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| NEWS | 6 | DEC 18 | MEDLINE updated in preparation for 2007 reload |
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| NEWS | 18 | FEB 23 | KOREAPAT enhanced with IPC 8 features and functionality |
| NEWS | 19 | FEB 26 | MEDLINE reloaded with enhancements |
| NEWS | 20 | FEB 26 | EMBASE enhanced with Clinical Trial Number field |
| NEWS | 21 | FEB 26 | TOXCENTER enhanced with reloaded MEDLINE |
| NEWS | 22 | FEB 26 | IFICDB/IFIPAT/IFIUDB reloaded with enhancements |
| NEWS | 23 | FEB 26 | CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases |
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L2 248 L1 AND PROTEOL?

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L3 142 DUP REM L2 (106 DUPLICATES REMOVED)

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L3 ANSWER 1 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

TI Mechanism of apoptosis induced by IFN- α in human myeloma cells: Role
of Jak1 and Bim and potentiation by rapamycin

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TI Adenoviral-mediated interferon α overcomes resistance to the interferon
protein in various cancer types and has marked bystander effects.

L3 ANSWER 3 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Methods for individually optimizing treatment for an inflammation-
associated disease

L3 ANSWER 4 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Use of gene expression data and other biochemical criteria in predicting
responsiveness to chemotherapy in breast cancer patients

L3 ANSWER 5 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Use of fusion proteins that can be taken up by skin cells to deliver
therapeutic macromolecules to the bloodstream without injection

L3 ANSWER 6 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Method for treating dementia or alzheimer's disease using a CD20 antibody

L3 ANSWER 7 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Genes showing altered levels of expression in pancreatic disease and their
use in diagnosis and prognosis of pancreatic cancer

L3 ANSWER 8 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Vaccinia virus infection attenuates innate immune responses and antigen presentation by epidermal dendritic cells

L3 ANSWER 9 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Viral and therapeutic control of IFN-beta promoter stimulator 1 during hepatitis C virus infection.

L3 ANSWER 10 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Chloroquine possesses a potent inhibitory effect of replication of HCV replicon.

L3 ANSWER 11 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI The C-terminal 26-residue peptide of serpin A1 is an inhibitor of HIV-1.

L3 ANSWER 12 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Differential gene induction by type I and type II Interferons and their combination.

L3 ANSWER 13 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Strategies to improve plasma half life time of peptide and protein drugs

L3 ANSWER 14 OF 142 MEDLINE on STN
 TI Hepatitis C virus NS2 and NS3/4A proteins are potent inhibitors of host cell cytokine/chemokine gene expression.

L3 ANSWER 15 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Induction of APOBEC3 family proteins, a defensive maneuver underlying interferon-induced anti-HIV-1 activity.

L3 ANSWER 16 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI TYK2 activity promotes ligand-induced IFNAR1 proteolysis.

L3 ANSWER 17 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Multiple sclerosis and virus induced immune responses: Autoimmunity can be primed by molecular mimicry and augmented by bystander activation.

L3 ANSWER 18 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Prospects of formulating proteins/peptides as aerosols for pulmonary drug delivery.

L3 ANSWER 19 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Hepatitis C virus NS2 and NS3/4A proteins are potent inhibitors of host cell cytokine/chemokine gene expression

L3 ANSWER 20 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Truncated sialyltransferase ST6GalNAc I polypeptides and nucleic acids

L3 ANSWER 21 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Truncated polypeptide N-acetylgalactosaminyltransferase II polypeptides and nucleic acids

L3 ANSWER 22 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Differentially expressed gene profile for diagnosing and treating mental disorders

L3 ANSWER 23 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Interferon Induces NF- κ B-inducing Kinase/Tumor Necrosis Factor Receptor-associated Factor-dependent NF- κ B Activation to Promote Cell Survival

L3 ANSWER 24 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5
 TI Crystal structure of the interferon-induced ubiquitin-like protein ISG15.

L3 ANSWER 25 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI High Serum Levels of Matrix Metalloproteinase-9 and Matrix Metalloproteinase-1 Are Associated with Rapid Progression in Patients with Metastatic Melanoma

L3 ANSWER 26 OF 142 MEDLINE on STN
 TI Enhancement of dendritic cell antigen cross-presentation by CpG DNA involves type I IFN and stabilization of class I MHC mRNA.

L3 ANSWER 27 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
 TI Engineering glycoprotein B of bovine herpesvirus 1 to function as transporter for secreted proteins: a new protein expression approach.

L3 ANSWER 28 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 7
 TI Intracellular domain of the IFN α 2 interferon receptor subunit mediates transcription via Stat2.

L3 ANSWER 29 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Regulated intramembrane proteolysis signaling by an interferon receptor.

L3 ANSWER 30 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 8
 TI TGF-beta 1 mRNA expression in liver biopsy specimens and TGF-beta 1 serum levels in patients with chronic hepatitis C before and after antiviral therapy.

L3 ANSWER 31 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 9
 TI Interferons induce proteolytic degradation of TRAILR4.

L3 ANSWER 32 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Involvement of PKR and RNase L in translational control and induction of apoptosis after Hepatitis C polyprotein expression from a vaccinia virus recombinant

L3 ANSWER 33 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 10
 TI Gene expression profiles and biomarkers for the detection of Chagas disease and other disease-related gene transcripts in blood

L3 ANSWER 34 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11
 TI Gene expression profiles and biomarkers for the detection of lung disease-related and other disease-related gene transcripts in blood

L3 ANSWER 35 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Transit peptide cleavage site sequences for production of plastid-targeted fusion proteins in plant cells

L3 ANSWER 36 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Cell surface polypeptides from Lactobacillus or Bifidobacterium and their use as immunomodulating probiotic compounds

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TI Gene expression profile of human and mouse genes in atopic dermatitis and psoriasis patients and its use for diagnosis, therapy, and drug screening
 L3 ANSWER 38 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning
 L3 ANSWER 39 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy
 L3 ANSWER 40 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Gann Monograph on Cancer Research:SPECIAL ISSUE IN COMMEMORATION OF THE 100TH ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH.
 L3 ANSWER 41 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Regulated proteolysis of the IFN α 2 subunit of the interferon-alpha receptor. DUPLICATE 12
 L3 ANSWER 42 OF 142 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
 TI [Soluble transferrin receptor concentration, interleukin 6 and 12 levels, alanine aminotransferase activity and viral load in children with chronic hepatitis C treated with interferon and ribavirine].
 STEZENIE ROZPUSZCZALNEGO RECEPTORA TRANSFERYNY, POZIOM INTERLEUKINY 6 I 12, AKTYWNOSC AMINOTRANSFERAZY ALANINOWEJ ORAZ WIREMIA U DZIECI Z PRZEWLEKLYM ZAPALENIEM WATROBY TYPU C LECZONYCH INTERFERONEM I RYBAWIRYNA.
 L3 ANSWER 43 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Diversity and Relatedness Among the Type I Interferons
 L3 ANSWER 44 OF 142 MEDLINE on STN
 TI Interferon therapy in chronic myelogenous leukemia.
 L3 ANSWER 45 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 13
 TI Undermining tumor angiogenesis by gene therapy: An emerging field
 L3 ANSWER 46 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 14
 TI A reporter-based assay for identifying hepatitis C virus inhibitors based on subgenomic replicon cells
 L3 ANSWER 47 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI An interferon receptor signals via regulated intramembrane proteolysis (RIP).
 L3 ANSWER 48 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy
 L3 ANSWER 49 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI SCFHOS ubiquitin ligase mediates the ligand-induced down-regulation of the interferon-alpha receptor. DUPLICATE 15
 L3 ANSWER 50 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Tissue remodelling in liver diseases. DUPLICATE 16
 L3 ANSWER 51 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Regulation of the expression and processing of caspase-12.

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 TI Development of a cell-based assay for monitoring specific hepatitis C virus NS3/4A protease activity in mammalian cells

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 TI Pathological mechanisms associated with CD34+ cell mobilization in idiopathic myelofibrosis.

L3 ANSWER 54 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Adhesion protein, protease, and protease inhibitor mutations and methods for diagnosis and treatment of epithelial cell adhesion-associated diseases

L3 ANSWER 55 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Long-acting cytokine derivatives and their pharmaceutical compositions

L3 ANSWER 56 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI In situ Langerhans cell vaccine

L3 ANSWER 57 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Therapeutic modulation of the tumor inflammatory response

L3 ANSWER 58 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

L3 ANSWER 59 OF 142 MEDLINE on STN
 TI Selective STAT protein degradation induced by paramyxoviruses requires both STAT1 and STAT2 but is independent of alpha/beta interferon signal transduction.

L3 ANSWER 60 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Microwave-enhanced enzyme reaction for protein mapping by mass spectrometry: A new approach to protein digestion in minutes. DUPLICATE 17

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 TI High expression levels of collagenase-1 and stromelysin-1 correlate with shorter disease-free survival in human metastatic melanoma.

L3 ANSWER 62 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Modulation of monocytes matrix metalloproteinase-2, MT1-MMP and TIMP-2 by interferon-alpha and -beta: Implications to multiple sclerosis.

L3 ANSWER 63 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Secretion of human interferon alpha 2b by Streptomyces lividans. DUPLICATE 18

L3 ANSWER 64 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI The nonstructural NS5A protein of hepatitis C virus: An expanding, multifunctional role in enhancing hepatitis C virus pathogenesis. DUPLICATE 19

L3 ANSWER 65 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Proteolytic degradation of the recombinant target protein, interferon- γ during its fermentative production in the methylotrophic yeast, *Pichia pastoris*

L3 ANSWER 66 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Production of IFNalpha-2a in *Hansenula polymorpha*. DUPLICATE 20

L3 ANSWER 67 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Post-translational modification of recombinant proteins in plants by altering its natural modification abilities

L3 ANSWER 68 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 21
 TI Prolonging the half-life of human interferon-alpha2 in circulation: Design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon-alpha2.

L3 ANSWER 69 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 22
 TI Virus infection induces proteolytic processing of IL-18 in human macrophages via caspase-1 and caspase-3 activation

L3 ANSWER 70 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Angiogenesis: Regulators and clinical applications.

L3 ANSWER 71 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI The V Protein of Human Parainfluenza Virus 2 Antagonizes Type I Interferon Responses by Destabilizing Signal Transducer and Activator of Transcription 2

L3 ANSWER 72 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Systems for oral delivery

L3 ANSWER 73 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Preparation of recombinant interferon- α lacking methionine residue at N-terminal

L3 ANSWER 74 OF 142 MEDLINE on STN
 TI Activity of growth factors in the IL-6 group in the differentiation of human lung adenocarcinoma.

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 TI Adoptive transfer from interferon- α -fed mice is associated with inhibition of active experimental autoimmune encephalomyelitis by decreasing recipient tumor necrosis factor- α secretion.

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 TI Expression of Flt3-ligand by the endothelial cell.

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 TI Combination therapy with glatiramer acetate (copolymer-1) and a type I interferon (IFN- α) does not improve experimental autoimmune encephalomyelitis.

L3 ANSWER 78 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Gene probes used for genetic profiling in healthcare screening and planning

L3 ANSWER 79 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Gene probes used for genetic profiling in healthcare screening and planning

L3 ANSWER 80 OF 142 MEDLINE on STN
 TI A dynamic connection between centromeres and ND10 proteins.

L3 ANSWER 81 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Inflammatory mediators regulate cathepsin S in macrophages and microglia:

a role in attenuating heparan sulfate interactions

- L3 ANSWER 82 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Hybrid (BDBB) interferon-alpha: Preformulation
studies.
- L3 ANSWER 83 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Therapeutic intervention with complement and β -glucan in cancer
- L3 ANSWER 84 OF 142 MEDLINE on STN
TI Tumour response and radiation-induced lung injury in patients with
recurrent small cell lung cancer treated with radiotherapy and concomitant
interferon-alpha.
- L3 ANSWER 85 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Identification of a linear epitope of interferon-alpha2b recognized by
neutralizing monoclonal antibodies.
- L3 ANSWER 86 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Protein-lipid vesicles and autogenous vaccine comprising the same
- L3 ANSWER 87 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Cloning and cDNA sequences of human interferon .alpha
./ β -binding proteins I and II and their pharmaceutical uses
- L3 ANSWER 88 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Effects of IFNalpha on late stages of HIV-1 replication cycle.
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TI Glucocorticoids and Th-1, Th-2 type cytokines in rheumatoid arthritis,
osteoarthritis, asthma, atopic dermatitis and AIDS.
- L3 ANSWER 90 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI The use of Wobenzym to facilitate interferon synthesis in the treatment of
chronic urogenital chlamydiosis.
- L3 ANSWER 91 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 29
TI Modulation of Apo-1/Fas (CD95)-induced programmed cell death in myeloma
cells by interferon-alpha-2.
- L3 ANSWER 92 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Conjugation of the 15-kDa interferon-induced ubiquitin homolog is distinct
from that of ubiquitin
- L3 ANSWER 93 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon-alpha/beta binding protein, its preparation
and use
- L3 ANSWER 94 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 30
TI The cytokines of inflammation.
- L3 ANSWER 95 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 31
TI Interferon-alpha-2b increases fibrolysis in fibrotic
livers from bile duct ligated rats: Possible participation of the
plasminogen activator.
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- TI Interferon increases extracellular matrix degradation and plasminogen activator activity in livers from cirrhotic rats.
- L3 ANSWER 97 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Resistance of recombinant proteins to proteolysis during folding and in the folded state
- L3 ANSWER 98 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
- TI Lipopolysaccharide (LPS), LPS-immune complexes and cytokines as inducers of pulmonary inflammation in patients with cystic fibrosis and chronic Pseudomonas aeruginosa lung infection.
- L3 ANSWER 99 OF 142 MEDLINE on STN
- TI Approaches to the development of novel inhibitors of hepatitis C virus replication.
- L3 ANSWER 100 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 32
- TI Modulation of THE bovine microvascular endothelial cell proteolytic properties by inhibitors of angiogenesis.
- L3 ANSWER 101 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 33
- TI Proteolytic enzymes and amylase induce cytokine production in human peripheral blood mononuclear cells in vitro.
- L3 ANSWER 102 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 34
- TI Interferon-alpha-2 counteracts interleukin-1-alpha-stimulated expression of urokinase-type plasminogen activator in human foreskin microvascular endothelial cells in vitro.
- L3 ANSWER 103 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Quantitation of interferon-induced Mx protein in whole blood lysates by an immunochemiluminescent assay: elimination of protease activity of cell lysates in toto
- L3 ANSWER 104 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 35
- TI Alpha- and gamma-interferon inhibit plasminogen activator inhibitor-1 gene expression in human retinal pigment epithelial cells
- L3 ANSWER 105 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 36
- TI Expression of human interferon-alpha-2 in Sf9 cells. Characterization of O-linked glycosylation and protein heterogeneities.
- L3 ANSWER 106 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Cytokine synthesis in human peripheral blood mononuclear cells after oral administration of polyenzyme preparations
- L3 ANSWER 107 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
- TI The human gene encoding tryptophanyl-tRNA synthetase: interferon-response elements and exon-intron organization
- L3 ANSWER 108 OF 142 MEDLINE on STN
- TI Soluble tumor necrosis factor receptor expression in patients with metastatic renal cell carcinoma treated with interleukin-2-based immunotherapy.
- L3 ANSWER 109 OF 142 MEDLINE on STN
- TI Tumor necrosis factor induction of endothelial cell urokinase-type plasminogen activator mediated proteolysis of extracellular matrix and its antagonism by gamma-interferon.

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TI Nerve lesions induced by macrophage activation.

L3 ANSWER 111 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Regulation of Staphylococcus protease using complement, interferon and
immunoglobulin as substrates

L3 ANSWER 112 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI [Ala IL-8] as a leukocyte adhesion inhibitor, and its recombinant
production, purification, and activity

L3 ANSWER 113 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Chemically synthesized gene provides in Escherichia coli cells for the
biosynthesis of a polypeptide, the structure of which corresponds to human
 $\alpha 2$ leukocyte interferon

L3 ANSWER 114 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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DUPLICATE 37
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.

L3 ANSWER 115 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 38
TI Mapping of an epitope of human leukocyte α interferon A which is
recognized by the murine monoclonal antibody NK2

L3 ANSWER 116 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structural analysis of recombinant proteins by fast atom bombardment and
californium-252 plasma desorption mass spectrometry

L3 ANSWER 117 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Charge heterogeneity of $\beta 2$ -microglobulin in lymphoid cells

L3 ANSWER 118 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structural organization of the interferon molecules as precursors of
immuno- and neuroactive oligopeptides

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DUPLICATE 39
TI SECRETORY EXPRESSION IN ESCHERICHIA-COLI AND BACILLUS-SUBTILIS OF HUMAN
INTERFERON ALPHA GENES DIRECTED BY STAPHYLOKINASE
SIGNALS.

L3 ANSWER 120 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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DUPLICATE 40
TI CELL SURFACE-ASSOCIATED PROTEINASES IN NK CELL-MEDIATED CYTOTOXICITY
ENHANCEMENT OF ENZYME EXPRESSION IS UNIQUE TO ACTIVATION WITH
INTERFERON-ALPHA.

L3 ANSWER 121 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lymphocytes treated with natural alpha-interferon produce a chemotactic
factor for human neutrophils

L3 ANSWER 122 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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DUPLICATE 41
TI LOW TEMPERATURES STABILIZE INTERFERON ALPHA-2 AGAINST
PROTEOLYSIS IN METHYLOPHILUS-METHYLOTROPHUS AND ESCHERICHIA-COLI.

L3 ANSWER 123 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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DUPLICATE 42
TI ACTIVATION OF PROTEIN BREAKDOWN AND PROSTAGLANDIN E-2 PRODUCTION IN RAT
SKELETAL MUSCLE IN FEVER IS SIGNALLED BY A MACROPHAGE PRODUCT DISTINCT FROM
INTERLEUKIN 1 OR OTHER KNOWN MONOKINES.

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DUPLICATE 43

TI STUDY OF OLIGOMERIC FORMS OF HUMAN LEUKOCYTE INTERFERONS OBTAINED BY GENE ENGINEERING TECHNIQUES.

L3 ANSWER 125 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Identification and partial characterization of a novel protease in *Saccharomyces cerevisiae* which cleaves the peptide bond between residues 22 and 23 in α -interferon, and identification of an α -interferon resistant to said proteolysis

L3 ANSWER 126 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Chemical characterization of recombinant human leukocyte interferon A using fast atom bombardment mass spectrometry

L3 ANSWER 127 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

TI INFLUENCE OF ENERGY SOURCE AND HEAT ON THE STABILITY OF HUMAN INTERFERON ALPHA-2 IN METHYLOPHILUS-METHYLOTROPHUS.

L3 ANSWER 128 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 44

TI PROTEOLYSIS IN THE OBLIGATE METHYLOTROPH METHYLOPHILUS-METHYLOTROPHUS.

L3 ANSWER 129 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 45

TI INTRACELLULAR DEGRADATION OF RECOMBINANT PROTEINS IN RELATION TO THEIR LOCATION IN ESCHERICHIA-COLI CELLS.

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TI 7. Isolation and purification of human alpha interferon, a recombinant DNA protein.

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TI High-performance liquid chromatography analysis of recombinant interferon- α 2 and interferon- α .2 analogue proteins purified by immunoabsorption chromatography

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TI Interferon secreted by *Bacillus subtilis* is retained by membranes

L3 ANSWER 133 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Chromatographic methods for purification of leukocyte interferon

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TI Modified (1-28) beta interferons

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TI COMPARATIVE IMMUNOCHEMICAL STUDY OF SOME HUMAN LEUKOCYTE INTERFERONS.

L3 ANSWER 136 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 47

TI LIMITED PROTEOLYSIS OF HUMAN LEUKOCYTE INTERFERON ALPHA-2 AND LOCALIZATION OF THE MONOCLONAL ANTIBODY BINDING ANTIGENIC DETERMINANT.

L3 ANSWER 137 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Secretion of foreign proteins from *Saccharomyces cerevisiae* directed by α -factor gene fusions

L3 ANSWER 138 OF 142 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 48

TI BIOLOGIC ACTIVITY IN A FRAGMENT OF RECOMBINANT HUMAN INTERFERON ALPHA.

L3 ANSWER 139 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI Mouse interferon receptors: a difference in their response to α and β interferons

L3 ANSWER 140 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 49

TI Interferon-mediated inhibition of production of Gazdar murine sarcoma virus, a retrovirus lacking env proteins and containing an uncleaved gag precursor

L3 ANSWER 141 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI A new mass-spectrometric C-terminal sequencing technique finds a similarity between γ -interferon and $\alpha 2$ -interferon and identifies a proteolytically clipped γ -interferon that retains full antiviral activity

L3 ANSWER 142 OF 142 CAPLUS COPYRIGHT 2007 ACS on STN

TI The kidney is the main site of interferon degradation

=> Log off H
 SESSION WILL BE HELD FOR 120 MINUTES
 STN INTERNATIONAL SESSION SUSPENDED AT 13:42:49 ON 25 MAR 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
 SESSION RESUMED IN FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE'
 AT 13:56:52 ON 25 MAR 2007
 FILE 'BIOSIS' ENTERED AT 13:56:52 ON 25 MAR 2007
 Copyright (c) 2007 The Thomson Corporation
 FILE 'CAPLUS' ENTERED AT 13:56:52 ON 25 MAR 2007
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 FILE 'MEDLINE' ENTERED AT 13:56:52 ON 25 MAR 2007

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 50.90 | 51.11 |

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(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007

L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT

L2 248 S L1 AND PROTEOL?

L3 142 DUP REM L2 (106 DUPLICATES REMOVED)

=> S L3 and Resistance

L4 21 L3 AND RESISTANCE

=> D Ti L4 1-24

L4 ANSWER 1 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Adenoviral-mediated interferon α overcomes resistance to the
 interferon protein in various cancer types and has marked bystander
 effects.

L4 ANSWER 2 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Gann Monograph on Cancer Research:SPECIAL ISSUE IN COMMEMORATION OF THE
 100TH ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH.

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Use of gene expression data and other biochemical criteria in predicting
 responsiveness to chemotherapy in breast cancer patients

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Genes showing altered levels of expression in pancreatic disease and their
 use in diagnosis and prognosis of pancreatic cancer

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Truncated polypeptide N-acetylgalactosaminyltransferase II polypeptides
 and nucleic acids

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Truncated sialyltransferase ST6GalNAc I polypeptides and nucleic acids

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Differentially expressed gene profile for diagnosing and treating mental
 disorders

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Sequences of human schizophrenia related genes and use for diagnosis,
 prognosis and therapy

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Gene expression profiles and biomarkers for the detection of Chagas
 disease and other disease-related gene transcripts in blood

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Gene expression profile of human and mouse genes in atopic dermatitis and
 psoriasis patients and its use for diagnosis, therapy, and drug screening

L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI High throughput directed evolution of proteins and peptides using
 two-dimensional rational mutagenesis scanning

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Ligand binding domains of cytokine which are linked via flexible
 polypeptide linker and uses in therapy

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Endocrine disruptor screening using DNA chips of endocrine
 disruptor-responsive genes

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Long-acting cytokine derivatives and their pharmaceutical compositions

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Gene probes used for genetic profiling in healthcare screening and
 planning

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Gene probes used for genetic profiling in healthcare screening and
 planning

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Therapeutic intervention with complement and β -glucan in cancer

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Cloning and cDNA sequences of human interferon .alpha
 ./β-binding proteins I and II and their pharmaceutical uses

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Interferon-alpha/beta binding protein, its preparation
 and use

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Resistance of recombinant proteins to proteolysis
 during folding and in the folded state

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Identification and partial characterization of a novel protease in
 Saccharomyces cerevisiae which cleaves the peptide bond between residues
 22 and 23 in α-interferon, and identification of an
 α-interferon resistant to said proteolysis

=> D Ibib ABS L4 1-21

L4 ANSWER 1 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 2007:206271 BIOSIS
 DOCUMENT NUMBER: PREV200700198033
 TITLE: Adenoviral-mediated interferon a overcomes
 resistance to the interferon protein in various
 cancer types and has marked bystander effects.
 AUTHOR(S): Zhang, X.; Yang, Z.; Dong, L.; Papageorgiou, A.; McConkey,
 D. J.; Benedict, W. F. [Reprint Author]
 CORPORATE SOURCE: Univ Texas, MD Anderson Canc Ctr, Dept Genitourinary Med
 Oncol, 1515 Holcombe Blvd, Box 1374, Houston, TX 77030 USA
 wbenedic@mdanderson.org
 SOURCE: Cancer Gene Therapy, (MAR 2007) Vol. 14, No. 3, pp.
 241-250.
 ISSN: 0929-1903.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 21 Mar 2007
 Last Updated on STN: 21 Mar 2007

AB We have previously shown that intravesical administration of adenovirus
 encoding human interferon alpha-2b (Ad-IFN) induced a
 marked regression of superficial human bladder tumors derived from cells
 that are resistant to over 1 million units/ml of IFN alpha protein in
 vitro. In addition, Ad-IFN appeared to produce strong bystander effects.
 In this study, we show that Ad-IFN causes marked inhibition of cell growth
 and apoptosis in cells of various tumor types, all of which are resistant
 to IFN alpha protein. In addition, strong perinuclear IFN staining was
 seen in all cell lines following Ad-IFN transfection and was never
 observed after exposure to the IFN protein. Ad-IFN induced
 proteolytic processing of caspases 3, 8 and 9, indicative of
 enzymatic activation. However, the caspase-8-selective inhibitor,
 IETDfmk, blocked apoptosis only in the cell lines that were sensitive to
 the IFN alpha protein and had minimal effect on Ad-IFN-induced caspase-3
 or -9 processing and cell death, indicating that death
 receptor-independent mechanism(s) were involved in the cytotoxic effects
 observed for cancer cell lines resistant to the IFN alpha protein.
 Moreover, we document that a yet to be identified soluble factor(s) is
 responsible for causing the bystander effect observed following Ad-IFN
 treatment in IFN protein-resistant cancer cells.

L4 ANSWER 2 OF 21 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 2006:165130 BIOSIS
 DOCUMENT NUMBER: PREV200600160152
 TITLE: Gann Monograph on Cancer Research:SPECIAL ISSUE IN

COMMEMORATION OF THE 100TH ANNIVERSARY OF THE LATE DR.
TOMIZO YOSHIDA'S BIRTH.

AUTHOR(S): Tsuruo, T [Editor]; Kitagawa, T [Editor]
SOURCE: Tsuruo, T [Editor]; Kitagawa, T [Editor]. Gann Monograph on
Cancer Research, (2004) Gann Monograph on Cancer
Research:SPECIAL ISSUE IN COMMEMORATION OF THE 100TH
ANNIVERSARY OF THE LATE DR. TOMIZO YOSHIDA'S BIRTH.
Publisher: JAPAN SCIENTIFIC SOC PRESS, 2-10 HONGO, 6-CHOME,
BUNKYO-KU, TOKYO, 113, JAPAN. Series: GANN MONOGRAPH ON
CANCER RESEARCH.
ISSN: 0072-0151. ISBN: 3-8055-7816-4 (H) .
DOCUMENT TYPE: Book
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Mar 2006
Last Updated on STN: 9 Mar 2006

AB This 280-page book, entitled 'Cancer Research Front of Japan, 2003' is
volume 52 of the Gann Monograph on Cancer Research Series and is a special
issue published in commemoration of the late Dr. Tomizo Yoshida's birth,
who initiated the first publication of this series in 1966. This volume
is structured into 4 major sections and contains 18 individually-authored
papers. The focus of the first section is pathology and there are 4
papers in this section that individually discuss: the isolation of
p53-target genes and their functional analysis; cell adhesion system and
human cancer morphogenesis; gastrointestinal stromal tumor as a model for
molecular-based diagnosis and treatment of solid tumors; and stem cells
and gastric cancer and the role of gastric and intestinal mixed intestinal
metaplasia. Carcinogenesis is the theme of the second section, which
contains 4 more specific papers. Topics covered in these 4 papers
include: renal carcinogenesis in terms of genotype, phenotype and
dramatype; heterocyclic amines as mutagens/carcinogens produced during the
cooking of meat and fish; a medium-term rat liver bioassay for rapid in
vivo detection of the carcinogenic potential of chemicals; and the
metabolic activation of polycyclic aromatic hydrocarbons to carcinogens by
cytochromes P450 1A1 and 1B1. Cell biology is the focus of the third
section, which contains 6 papers on the topic. These 6 papers
individually discuss: NK4 in cancer biology and therapeutics; new aspects
of interferon-alpha/beta (IFN-alpha/beta) signaling in
immunity, oncogenesis and bone metabolism; tumor formation by genetic
mutations of beta-catenin, APC, and axin in the Wnt signaling pathway;
regulation of transforming growth factor-beta (TGF-beta) signaling and its
roles in tumor progression; vascular endothelial growth factor (VEGF)
receptor-2 and its unique signaling and specific ligand, VEGF-2; and the
roles of pericellular proteolysis by membrane type-1 matrix
metalloproteinase in cancer invasion and angiogenesis. The final section
concentrates on chemotherapy and the 4 papers in this section individually
discuss the antitumor activity of sugar-modified cytosine nucleosides;
molecular targeting therapy of cancer in terms of drug resistance
, apoptosis and survival signal; the basic and clinical implications of
ABC transporters, Y-box-binding protein-1 (YB-1) and angiogenesis-related
factors in human malignancies; and molecular mechanisms of angiogenesis in
non-small cell lung cancer, and therapeutics targeting related molecules.
The book is indexed by author and by subject, and contains 59 figures, 18
of which are in color, and 16 tables. This book will be of interest to
oncologists, tumor biology researchers, cell biologists, toxicologists,
pathologists and pharmacologists.

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:795782 CAPLUS

DOCUMENT NUMBER: 145:208138

TITLE: Use of gene expression data and other biochemical
criteria in predicting responsiveness to chemotherapy
in breast cancer patients

INVENTOR(S): Dai, Hongyue; Friend, Stephen H.; Deutsch, Paul

PATENT ASSIGNEE(S): Rosetta Inpharmatics LLC, USA; Merck & Co., Inc.

SOURCE: PCT Int. Appl., 349pp.

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

CODEN: PIXXD2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2006084272 | A2 | 20060810 | WO 2006-US4280 | 20060206 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |

PRIORITY APPLN. INFO.: US 2005-650365P P 20050204

AB A method of predicting the responsiveness of a breast cancer patient to chemotherapy using a combination of biochem. criteria, especially estrogen receptor levels, age, and gene expression profiles is described. The invention also provides a method for selecting patients for enrollment in a clin. trial of a drug for treating breast cancer based on these factors. Methods of statistical anal. and integration of these data are described.

L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:238155 CAPLUS

DOCUMENT NUMBER: 144:310062

TITLE: Genes showing altered levels of expression in pancreatic disease and their use in diagnosis and prognosis of pancreatic cancer

INVENTOR(S): Kloeppe, Guenter; Luettgies, Jutta; Kalthoff, Holger; Ammerpohl, Ole; Gruetzmann, Robert; Pilarsky, Christian; Saeger, Hans Detlev; Alldinger, Ingo

PATENT ASSIGNEE(S): Technische Universitaet Dresden, Germany

SOURCE: Ger. Offen., 132 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------|--|----------|----------------------|----------|
| DE 102004042822 | A1 | 20060316 | DE 2004-102004042822 | 20040831 |
| WO 2006024283 | A2 | 20060309 | WO 2005-DE1527 | 20050826 |
| WO 2006024283 | A3 | 20060831 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |

PRIORITY APPLN. INFO.: DE 2004-102004042822A 20040831

AB Genes showing altered levels of expression in healthy vs. neoplastic

pancreas are identified for use in the diagnosis of cancers including ductal adenocarcinoma; as indicators in screening for effective drugs; and as targets for nucleic acid-based therapies including antisense nucleic acids or siRNA. Gene expression profiling identified 1419 genes showing changes in levels of expression in neoplastic epithelium of which 650 were up-regulated and 769 were down-regulated. Of the 1419 genes, 1267 were not previously known to have any connection with pancreatic neoplasms.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1330475 CAPLUS

DOCUMENT NUMBER: 144:65957

TITLE: Truncated polypeptide N-acetylgalactosaminyltransferase II polypeptides and nucleic acids

INVENTOR(S): Johnson, Karl F.; Chen, Xi; Taudte, Susann; Saribas, Sami

PATENT ASSIGNEE(S): Neose Technologies, Inc., USA

SOURCE: PCT Int. Appl., 123 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2005121331 | A2 | 20051222 | WO 2005-US19442 | 20050603 |
| WO 2005121331 | A8 | 20060309 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2004-546530P P 20040603
US 2004-598584P P 20040803

AB The present invention features compns. and methods related to mutants of human polypeptide N-acetylgalactosaminyltransferase II (GalNAcT2) that are truncated by deletion of the N-terminal 1-40, 1-73, or 1-94 residues. Truncated forms of GalNAcT2 possess biol. activities comparable to, and in some instances, in excess of their full-length polypeptide counterparts, and may have enhanced properties of solubility, stability, and resistance to proteolytic degradation. GalNAcT2 is an essential reagent for glycosylation of therapeutic glycopeptides and oligosaccharides. The invention also features nucleic acids encoding such truncated polypeptides, as well as vectors, host cells, expression systems, and methods of expressing and using such polypeptides.

L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1330319 CAPLUS

DOCUMENT NUMBER: 144:65956

TITLE: Truncated sialyltransferase ST6GalNAc I polypeptides and nucleic acids

INVENTOR(S): Johnson, Karl F.; Hakes, David; Wei, Ge; Liu, Li; Saribas, Sami; Sjoberg, Eric; Clausen, Henrik; Bennett, Eric Paul; Mobasser, Aliakbar

PATENT ASSIGNEE(S): Neose Technologies, Inc., USA

SOURCE: PCT Int. Appl., 192 pp.

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

CODEN: PIXXD2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005121332 | A2 | 20051222 | WO 2005-US19583 | 20050603 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2004-576433P P 20040603
US 2005-650011P P 20050204

AB The present invention features compns. and methods related to mutants of human, murine, and chicken CMP-acetylneuraminase- α -acetylglactosaminide α 2 \rightarrow 6-sialyltransferase (ST6GalNAcI) that are truncated by deletion of N-terminal residues. Truncated forms of ST6GalNAcI possess biol. activities comparable to, and in some instances, in excess of their full-length polypeptide counterparts, and may have enhanced properties of solubility, stability, and resistance to proteolytic degradation. ST6GalNAcI is an essential reagent for glycosylation of therapeutic glycopeptides and oligosaccharides. The invention also features nucleic acids encoding such truncated polypeptides, as well as vectors, host cells, expression systems, and methods of expressing and using such polypeptides.

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:447673 CAPLUS

DOCUMENT NUMBER: 143:20875

TITLE: Differentially expressed gene profile for diagnosing and treating mental disorders

INVENTOR(S): Akil, Huda; Atz, Mary; Bunney, William E., Jr.; Choudary, Prabhakara V.; Evans, Simon J.; Jones, Edward G.; Li, Jun; Lopez, Juan F.; Myers, Richard; Thompson, Robert C.; Tomita, Hiroaki; Vawter, Marquis P.; Watson, Stanley

PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA

SOURCE: PCT Int. Appl., 226 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2005046434 | A2 | 20050526 | WO 2004-US36784 | 20041105 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, | | | |

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 2005209181 A1 20050922 US 2004-982556 20041104
AU 2004289247 A1 20050526 AU 2004-289247 20041105
CA 2543811 A1 20050526 CA 2004-2543811 20041105
EP 1680009 A2 20060719 EP 2004-800741 20041105

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
HR, IS, YU

PRIORITY APPLN. INFO.: US 2003-517751P P 20031105
US 2004-982556 A 20041104
WO 2004-US36784 W 20041105

AB The present invention provides methods for diagnosing mental disorders (e.g., psychotic disorders such as schizophrenia). The present invention uses DNA microarray anal. to demonstrate differential expression of genes in selected regions of post-mortem brains from patients diagnosed with mental disorders in comparison with normal control subjects. The invention also provides methods of identifying modulators of such mental disorders as well as methods of using these modulators to treat patients suffering from such mental disorders.

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:248643 CAPLUS

DOCUMENT NUMBER: 142:274056

TITLE: Sequences of human schizophrenia related genes and use for diagnosis, prognosis and therapy

INVENTOR(S): Liew, Choong-Chin

PATENT ASSIGNEE(S): Chondrogene Limited, Can.

SOURCE: U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 47

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241727 | A1 | 20041202 | US 2004-812731 | 20040330 |

PRIORITY APPLN. INFO.: US 1999-115125P P 19990106
US 2000-477148 B1 20000104
US 2002-268730 A2 20021009
US 2003-601518 A2 20030620
US 2004-802875 A2 20040312
US 2004-812731 A 20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing and monitoring diseases using gene-specific and/or tissue-specific primers. The present invention also describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:139371 CAPLUS
DOCUMENT NUMBER: 142:195820
TITLE: Gene expression profiles and biomarkers for the
detection of Chagas disease and other disease-related
gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): ChondroGene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S.
Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2004241729 | A1 | 20041202 | US 2004-813097 | 20040330 |
| US 2004014059 | A1 | 20040122 | US 2002-268730 | 20021009 |
| US 2005191637 | A1 | 20050901 | US 2004-803737 | 20040318 |
| US 2005196762 | A1 | 20050908 | US 2004-803759 | 20040318 |
| US 2005196763 | A1 | 20050908 | US 2004-803857 | 20040318 |
| US 2005196764 | A1 | 20050908 | US 2004-803858 | 20040318 |
| US 2005208505 | A1 | 20050922 | US 2004-803648 | 20040318 |
| US 2004241729 | A1 | 20041202 | US 2004-813097 | 20040330 |
| PRIORITY APPLN. INFO.: | | | US 1999-115125P | P 19990106 |
| | | | US 2000-477148 | B1 20000104 |
| | | | US 2002-268730 | A2 20021009 |
| | | | US 2003-601518 | A2 20030620 |
| | | | US 2004-802875 | A2 20040312 |
| | | | US 2004-813097 | A 20040330 |

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular Chagas disease, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen. [This abstract record is one of 3 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:308529 CAPLUS
DOCUMENT NUMBER: 140:333599
TITLE: Gene expression profile of human and mouse genes in
atopic dermatitis and psoriasis patients and its use
for diagnosis, therapy, and drug screening
INVENTOR(S): Itoh, Mikito; Ogawa, Kaoru; Shinagawa, Akira; Sudo,
Hajime; Ogawa, Hideoki; Ra, Chisei; Mitsuishi, Kouichi
PATENT ASSIGNEE(S): Genox Research, Inc., Japan; Juntendo University
SOURCE: PCT Int. Appl., 611 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004031386 | A1 | 20040415 | WO 2003-JP9808 | 20030801 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003252326 | A1 | 20040423 | AU 2003-252326 | 20030801 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | JP 2002-229318 | A 20020806 |
| | | | JP 2003-136543 | A 20030514 |
| | | | WO 2003-JP9808 | W 20030801 |
| AB This invention provides gene expression profile between a rash site and a no-rash site in a patient with atopic dermatitis or a patient with psoriasis. The invention also provides gene expression profile between a no-rash site in such a disease and a normal subject. Animal models, particularly mouse for those diseases are also claimed. The gene expression profile provided in this invention can be used for diagnosis, therapy, and drug screening for atopic dermatitis and psoriasis. | | | | |
| REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | | |
| L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN | | | | |
| ACCESSION NUMBER: 2004:220463 CAPLUS | | | | |
| DOCUMENT NUMBER: 140:265579 | | | | |
| TITLE: High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning | | | | |
| INVENTOR(S): Gantier, Rene; Guyon, Thierry; Cruz Ramos, Hugo; Vega, Manuel; Drittanti, Lila | | | | |
| PATENT ASSIGNEE(S): Nautilus Biotech, Fr. | | | | |
| SOURCE: PCT Int. Appl., 431 pp. | | | | |
| CODEN: PIXXD2 | | | | |
| DOCUMENT TYPE: Patent | | | | |
| LANGUAGE: English | | | | |
| FAMILY ACC. NUM. COUNT: 2 | | | | |
| PATENT INFORMATION: | | | | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2004022747 | A1 | 20040318 | WO 2003-IB4255 | 20030908 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2498284 | A1 | 20040318 | CA 2003-2498284 | 20030908 |
| AU 2003267700 | A1 | 20040329 | AU 2003-267700 | 20030908 |
| EP 1539950 | A1 | 20050615 | EP 2003-748392 | 20030908 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2005202438 | A1 | 20050915 | US 2003-658355 | 20030908 |
| US 2006020396 | A1 | 20060126 | US 2005-196067 | 20050802 |

PRIORITY APPLN. INFO.:

US 2002-410258P P 20020909
 US 2003-457063P P 20030321
 US 2002-409898P P 20020909
 US 2003-457135P P 20030321
 US 2003-658355 A1 20030908
 WO 2003-IB4255 W 20030908

AB The invention claims processes and systems for the high throughput directed evolution of peptides and proteins. It also provides a rational method for generating protein variants. The method relies on an indirect search for protein improvement for a particular activity, such as increased resistance to proteolysis, based on a rational amino acid replacement and sequence change at single or a limited number of amino acid positions at a time. The target amino acids are selected in silico for replacement and are referred to as "is-HIT target positions". The collection (or library) of all is-HITs represents the first dimension (target residue position) of the two-dimensional scanning methods. The second dimension is the replacing amino acids. The collection of mutant mols., or in silico candidate LEADS, is generated, tested and phenotypically characterized one-by-one, for example in addressable arrays. Optimized proteins having modified amino acid sequences at some regions along the protein that perform better than the starting sequence are identified and isolated. The methods were applied to interferon α -2b and interferon- β to obtain mutants with altered resistance to proteolysis and/or higher conformational stability.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:591215 CAPLUS

DOCUMENT NUMBER: 139:144956

TITLE: Ligand binding domains of cytokine which are linked via flexible polypeptide linker and uses in therapy

INVENTOR(S): Ross, Richard; Artymiuk, Peter; Sayers, Jon

PATENT ASSIGNEE(S): Asterion Limited, UK

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|--|----------|-----------------|----------|
| WO 2003062276 | A2 | 20030731 | WO 2003-GB253 | 20030124 |
| WO 2003062276 | A3 | 20031016 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2510751 | A1 | 20030731 | CA 2003-2510751 | 20030124 |
| EP 1468020 | A2 | 20041020 | EP 2003-702702 | 20030124 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| JP 2005529583 | T | 20051006 | JP 2003-562153 | 20030124 |
| IN 2004KN00972 | A | 20060505 | IN 2004-KN972 | 20040713 |
| BR 2004003173 | A | 20060321 | BR 2004-3173 | 20040730 |
| US 2005214762 | A1 | 20050929 | US 2005-502344 | 20050511 |
| US 2007054364 | A1 | 20070308 | US 2006-595991 | 20061113 |

PRIORITY APPLN. INFO.: GB 2002-1679 A 20020125
 WO 2003-GB253 W 20030124
 US 2005-502344 B3 20050511

AB The invention relates to the provision of oligomeric polypeptides (dimers, trimers, etc) comprising the ligand binding domains of cytokines which are linked via flexible polypeptide linker mols. The linker mols. optionally comprise protease sensitive sites to modulate the release of biol. active cytokines when administered to a human or animal subject. The invention also relates to chemical crosslinkers wherein the chemical crosslinkers serve to link the ligand binding domains. The chimeric cytokine can be used for treating acromegaly, gigantism, GH deficiency, Turners syndrome, renal failure, osteoporosis, diabetes mellitus, cancer, obesity, insulin resistance, hyperlipidemia, hypertension, anemia, autoimmune and infectious disease, inflammatory disorders including rheumatoid arthritis.

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:937303 CAPLUS
 DOCUMENT NUMBER: 138:20443
 TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
 INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
 PATENT ASSIGNEE(S): Takara Bio Inc., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| JP 2002355079 | A | 20021210 | JP 2002-69354 | 20020313 |
| PRIORITY APPLN. INFO.: | | | JP 2001-73183 | A 20010314 |
| | | | JP 2001-74993 | A 20010315 |
| | | | JP 2001-102519 | A 20010330 |

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17- β estradiol (E2), were found in mice by DNA chip anal.

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:353234 CAPLUS
 DOCUMENT NUMBER: 136:359632
 TITLE: Long-acting cytokine derivatives and their pharmaceutical compositions
 INVENTOR(S): Shechter, Yoram; Fridkin, Matityahu; Goldwaser, Itzhak
 PATENT ASSIGNEE(S): Yeda Research and Development Co., Ltd., Israel
 SOURCE: PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002036067 | A2 | 20020510 | WO 2001-IL1005 | 20011030 |
| WO 2002036067 | A3 | 20030109 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002014223 | A5 | 20020515 | AU 2002-14223 | 20011030 |
| EP 1337270 | A2 | 20030827 | EP 2001-982682 | 20011030 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004131586 | A1 | 20040708 | US 2003-415668 | 20030902 |
| PRIORITY APPLN. INFO.: | | | IL 2000-139400 | A 20001101 |
| | | | WO 2001-IL1005 | W 20011030 |

AB Cytokine derivs. are provided bearing functional groups sensitive to mild basic conditions, such as fluorenylmethoxycarbonyl (Fmoc) and 2-sulfo-9-fluorenylmethoxycarbonyl (FMS), and pharmaceutical compns. comprising them. Preferred derivs. are those in which amino groups of the cytokine are substituted with FMS, for example FMS7-IFN- α 2 and FMS3-IL-2. These cytokine derivs. can be administered as inactive or slightly active prodrugs and are capable of undergoing spontaneous regeneration into the parent bioactive drugs under in vivo physiol. conditions and in a homogeneous fashion. The cytokine prodrugs present higher metabolic stability and augmented bioavailability. For example, in an in vivo experiment designed for the evaluation of the anti-metastatic capacity of FMS3-IL-2, mice were inoculated i.v. on day (-3) with 105 D122 metastatic cells. Native IL-2 and FMS3-IL-2 were administered i.p. at high and moderate concns. (5000 ng and 500 ng, resp.) once daily for 30 days. Each group consists of 8 mice. The original protocol for anti-metastatic therapy implies identical dosages given twice a day. However, since prolongation of FMS3-IL-2 in serum is assumed, it is administered only once a day. Metastatic load in lungs of mice was weighed on day 30.

L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:795994 CAPLUS
 DOCUMENT NUMBER: 132:31744
 TITLE: Gene probes used for genetic profiling in healthcare screening and planning
 INVENTOR(S): Roberts, Gareth Wyn
 PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK
 SOURCE: PCT Int. Appl., 745 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9964627 | A2 | 19991216 | WO 1999-GB1780 | 19990604 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, | | | | |

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

| | | |
|---------------|---|----------|
| GB 1998-12099 | A | 19980606 |
| GB 1998-13291 | A | 19980620 |
| GB 1998-13611 | A | 19980624 |
| GB 1998-13835 | A | 19980627 |
| GB 1998-14110 | A | 19980701 |
| GB 1998-14580 | A | 19980707 |
| GB 1998-15438 | A | 19980716 |
| GB 1998-15574 | A | 19980718 |
| GB 1998-15576 | A | 19980718 |
| GB 1998-16085 | A | 19980724 |
| GB 1998-16086 | A | 19980724 |
| GB 1998-16921 | A | 19980805 |
| GB 1998-17097 | A | 19980807 |
| GB 1998-17200 | A | 19980808 |
| GB 1998-17632 | A | 19980814 |
| GB 1998-17943 | A | 19980819 |

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:795993 CAPLUS
DOCUMENT NUMBER: 132:31743
TITLE: Gene probes used for genetic profiling in healthcare screening and planning
INVENTOR(S): Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9964626 | A2 | 19991216 | WO 1999-GB1779 | 19990604 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, | | | | |

DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|----|----------|-----------------|-------------|
| CA 2330929 | A1 | 19991216 | CA 1999-2330929 | 19990604 |
| AU 9941586 | A | 19991230 | AU 1999-41586 | 19990604 |
| AU 766544 | B2 | 20031016 | | |
| AU 9941587 | A | 19991230 | AU 1999-41587 | 19990604 |
| GB 2339200 | A | 20000119 | GB 1999-12914 | 19990604 |
| GB 2339200 | B | 20010912 | | |
| EP 1084273 | A1 | 20010321 | EP 1999-925207 | 19990604 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2003528564 | T | 20030930 | JP 2000-553616 | 19990604 |
| US 2003198970 | A1 | 20031023 | US 2002-206568 | 20020729 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | GB 1998-12098 | A 19980606 |
| | | | GB 1998-28289 | A 19981223 |
| | | | GB 1998-16086 | A 19980724 |
| | | | GB 1998-16921 | A 19980805 |
| | | | GB 1998-17097 | A 19980807 |
| | | | GB 1998-17200 | A 19980808 |
| | | | GB 1998-17632 | A 19980814 |
| | | | GB 1998-17943 | A 19980819 |
| | | | US 1999-325123 | B1 19990603 |
| | | | WO 1999-GB1779 | W 19990604 |

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the number of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide critical clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:360183 CAPLUS

DOCUMENT NUMBER: 131:183492

TITLE: Therapeutic intervention with complement and β -glucan in cancer

AUTHOR(S): Ross, Gordon D.; Vetvicka, Vaclav; Yan, Jun; Xia, Yu; Vetvickova, Jana

CORPORATE SOURCE: Department of Microbiology and Immunology, Department of Pathology, Division of Experimental Immunology and Immunopathology, University of Louisville, Louisville, KY, USA

SOURCE: Immunopharmacology (1999), 42(1-3), 61-74
CODEN: IMMUDP; ISSN: 0162-3109

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion with many refs. Complement (C) has two major effector systems available for host defense. The membrane attack complex

(MAC) generated from components C5-C9 can form membrane-penetrating lesions that lead to cell death by causing a rapid loss of cytoplasmic components. The MAC is only effective against pathogens with outer phospholipid membranes, and cannot kill Gram-pos. bacteria or yeast whose membranes are protected by cell walls. The most important effector mechanism of C is the opsonization of microbial pathogens with the serum protein C3 that leads to their high avidity attachment to the C3-receptors of phagocytic cells. Pathogens that activate complement are first coated with the C3b fragment of C3, which is rapidly proteolyzed into the iC3b fragment by serum factor I. These iC3b fragments serve to promote the high avidity attachment of the 'iC3b-opsonized' pathogens to the iC3b-receptors (CR3, CD11b/CD18) of phagocytic cells and natural killer (NK) cells, stimulating phagocytosis and/or cytotoxic degranulation. Host cells, including neoplastic tumor cells, have been endowed with natural mechanisms for self-protection against both the MAC and the cytotoxic activation of CR3. This review discusses a novel type of immunotherapy for cancer that uses soluble yeast β -glucan to override the normal resistance of iC3b-opsonized tumor cells to the cytotoxic activation of phagocyte and NK cell CR3, allowing this important effector mechanism of the C system to function against tumor cells in the same way that it normally functions against bacteria and yeast. Moreover, the cytotoxic activation of β -glucan-primed NK cell CR3 by iC3b-opsonized tumors is shown to be accompanied by a tumor-localized secretion of the cytokines TNF α , IFN α , IFN γ , and IL-6.

REFERENCE COUNT: 116 THERE ARE 116 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:667965 CAPLUS

DOCUMENT NUMBER: 129:299458

TITLE: Cloning and cDNA sequences of human interferon α / β -binding proteins I and II and their pharmaceutical uses

INVENTOR(S): Novick, Daniela; Cohen, Batya; Rubinstein, Menachem

PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel

SOURCE: U.S., 35 pp., Cont.-in-part of U.S. Ser. No. 115,741, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 5821078 | A | 19981013 | US 1995-385191 | 19950207 |
| US 6458932 | B1 | 20021001 | US 1995-472402 | 19950607 |
| JP 2004254695 | A | 20040916 | JP 2004-90279 | 20040325 |
| JP 2005162762 | A | 20050623 | JP 2005-4934 | 20050112 |
| JP 2005200422 | A | 20050728 | JP 2005-33495 | 20050209 |
| PRIORITY APPLN. INFO.: | | | IL 1992-103052 | A 19920903 |
| | | | IL 1993-106591 | A 19930804 |
| | | | US 1993-115741 | B2 19930903 |
| | | | IL 1994-108584 | A 19940207 |
| | | | JP 1993-243987 | A3 19930902 |
| | | | JP 1995-43539 | A3 19950207 |
| | | | US 1995-385191 | A3 19950207 |

AB Interferon α / β binding proteins are provided, which are capable of modulating the activity of interferon- α subtypes as well as interferon- β . Cloning of DNA mols. encoding these proteins, expression in host cells and antibodies against the proteins are also provided. Type I interferons (IFN- α and IFN- β and IFN- ω) are a family of cytokines usually defined by their ability to confer

resistance to viral infections. There are pathol. situations, related to these cytokines where neutralization of interferon activity may be beneficial to the patient. Cytokine-binding proteins (soluble cytokine receptors) correspond to the extracellular ligand binding domains of their resp. cell surface cytokine receptors. They are derived either by alternative splicing of pre-mRNA common to the cell surface receptor, or by proteolytic cleavage of the cell surface receptor. Therefore interferon α / β binding proteins were targeted that are capable of modulating the activity of interferon-. alpha. subtypes as well as interferon- β .

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:91925 CAPLUS

DOCUMENT NUMBER: 124:139220

TITLE: Interferon-alpha/beta binding protein, its preparation and use

INVENTOR(S): Cohen, Batya; Novick, Daniela; Rubinstein, Menachem

PATENT ASSIGNEE(S): Israel

SOURCE: Can. Pat. Appl., 85 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| CA 2141747 | A1 | 19950808 | CA 1995-2141747 | 19950203 |
| AU 9511416 | A | 19950817 | AU 1995-11416 | 19950127 |
| AU 688430 | B2 | 19980312 | | |
| FI 9500516 | A | 19950808 | FI 1995-516 | 19950206 |
| NO 9500420 | A | 19950808 | NO 1995-420 | 19950206 |
| NO 318912 | B1 | 20050523 | | |
| EP 676413 | A2 | 19951011 | EP 1995-101560 | 19950206 |
| EP 676413 | A3 | 19960403 | | |
| EP 676413 | B1 | 20050105 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| RU 2232811 | C2 | 20040720 | RU 1995-101848 | 19950206 |
| AT 286509 | T | 20050115 | AT 1995-101560 | 19950206 |
| PT 676413 | T | 20050531 | PT 1995-101560 | 19950206 |
| ES 2236696 | T3 | 20050716 | ES 1995-101560 | 19950206 |
| CN 1109505 | A | 19951004 | CN 1995-100194 | 19950207 |
| ZA 9500968 | A | 19951010 | ZA 1995-968 | 19950207 |
| JP 07298886 | A | 19951114 | JP 1995-43539 | 19950207 |
| JP 3670045 | B2 | 20050713 | | |
| JP 2005200422 | A | 20050728 | JP 2005-33495 | 20050209 |
| PRIORITY APPLN. INFO.: | | | IL 1994-108584 | A 19940207 |
| | | | JP 1995-43539 | A3 19950207 |

AB Type I interferons (IFN- α and IFN- β and IFN- ω) are a family of cytokines usually defined by their ability to confer resistance to viral infections. There are pathol. situations, related to these cytokines where neutralization of interferon activity may be beneficial to the patient. Cytokine binding proteins (soluble cytokine receptors) correspond to the extracellular ligand binding domains of their resp. cell surface cytokine receptors. They are derived either by alternative splicing of pre-mRNA common to the cell surface receptor, or by proteolytic cleavage of the cell surface receptor. Therefore interferon α / β binding proteins were targeted that are capable of modulating the activity of interferon-. alpha. subtypes as well as interferon- β . Cloning of DNA mols. encoding these proteins and expression in host cells and antibodies against these proteins is discussed.

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:332388 CAPLUS
DOCUMENT NUMBER: 122:104011
TITLE: Resistance of recombinant proteins to
proteolysis during folding and in the folded
state
AUTHOR(S): Fountoulakis, Michael
CORPORATE SOURCE: Dep. of Biology, F. Hoffmann-La Roche Ltd., Basel,
CH-4002, Switz.
SOURCE: Journal of Chemical Technology & Biotechnology (1995),
62(1), 81-90
CODEN: JCTBED; ISSN: 0268-2575
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protein purification often involves the use of denaturing agents for solubilization. During refolding, following removal of the denaturants, the proteins of interest are exposed to proteases present in the expression system. Here the resistance of selected recombinant proteins to three widely used proteolytic enzymes, trypsin (EC 3.4.21.4), proteinase K (EC 3.4.21.14) and endoproteinase Glu-C (EC 3.4.21.19), was investigated during folding and in the folded state. Target proteins and protease mixts. were denatured in 8 mol dm⁻³ urea and the proteins were allowed to refold by removal of the urea by dialysis. The proteolytic products were analyzed by sodium dodecyl sulfate-polyacrylamide gels and protein digestion during folding was compared with the digestion under similar conditions in physiol. buffer. Depending on the folding state of the proteins, the proteases had different effects on the substrates. During folding, certain recombinant proteins were more efficiently digested by trypsin and, in particular, by proteinase K in comparison with digestion in the folded state, while other protein substrates were more resistant to proteolytic degradation in a denatured or partially denatured state than their folded counterparts. Incubation of most substrate proteins with endoproteinase Glu-C yielded kinetics of digestion that were essentially similar for both partially folded and unfolded substrates. The results reported may be useful for protection of sensitive proteins and in studies of protein folding mechanisms.

L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:144742 CAPLUS
DOCUMENT NUMBER: 108:144742
TITLE: Identification and partial characterization of a novel
protease in *Saccharomyces cerevisiae* which cleaves the
peptide bond between residues 22 and 23 in
 α -interferon, and identification of an
 α -interferon resistant to said
proteolysis
INVENTOR(S): O'Loughlin, John T.
PATENT ASSIGNEE(S): Interferon Sciences, Inc., USA
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| EP 240224 | A2 | 19871007 | EP 1987-302519 | 19870324 |
| EP 240224 | A3 | 19890201 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| DK 8701614 | A | 19871001 | DK 1987-1614 | 19870330 |
| CN 87102497 | A | 19871111 | CN 1987-102497 | 19870330 |
| JP 62296892 | A | 19871224 | JP 1987-74566 | 19870330 |

PRIORITY APPLN. INFO.:

US 1986-845937

A 19860331

AB A novel *S. cerevisiae* protease cleaves α -interferons between basic amino acids at positions 22 and 23, but cleavage does not occur if residue 22 is serine. A recombinant interferon α with serine, threonine, asparagine, glutamine, or glycine at position 22 could be produced intact in a microorganism whose primary proteolytic activity against the natural species is at that site. The protease was partially purified from a protease-deficient PEP 3-4 *S. cerevisiae* mutant. It was membrane-bound and activated by the Triton X-100 present during cell lysis. Recombinant interferons α -1, α -2, and α -8 were all incubated with the protease. Both α -2 and α -8 were cleaved between amino acids 22 and 23 (which were Arg-Lys and Arg-Arg, resp.), but α -1 (Ser-Arg) was not.

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STN INTERNATIONAL SESSION SUSPENDED AT 13:58:52 ON 25 MAR 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *

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AT 14:18:26 ON 25 MAR 2007

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FILE 'MEDLINE' ENTERED AT 14:18:26 ON 25 MAR 2007

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SESSION

FULL ESTIMATED COST

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121.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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-14.82

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(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007

L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTIN OR VARIANT OR MUT

L2 248 S L1 AND PROTEOL?

L3 142 DUP REM L2 (106 DUPLICATES REMOVED)

L4 21 S L3 AND RESISTANCE

=> S L1 AND (IFN -alpha 2b)

L5 2141 L1 AND (IFN -ALPHA 2B)

=> S L5 AND Proteol?

L6 7 L5 AND PROTEOL?

=> Dup Rem 16

PROCESSING COMPLETED FOR L6

L7 3 DUP REM L6 (4 DUPLICATES REMOVED)

=> D ti L7 1-3

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

TI High throughput directed evolution of proteins and peptides using two-dimensional rational mutagenesis scanning

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

TI Identification of a linear epitope of interferon-.alpha.2b recognized by neutralizing monoclonal antibodies

L7 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2

TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.

=> D Ibib ABs L7 2,3

L7 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 1999:656689 CAPLUS

DOCUMENT NUMBER: 132:11491

TITLE: Identification of a linear epitope of interferon- α 2b recognized by neutralizing monoclonal antibodies

AUTHOR(S): Blank, Viviana C.; Sterin-Prync, Aida; Retegui, Lilia; Vidal, Alejandro; Criscuolo, Marcelo; Roguin, Leonor P.

CORPORATE SOURCE: Instituto de Quimica y Fisicoquimica Biologicas (UBA-CONICET), Facultad de Farmacia y Bioquimica, Buenos Aires, 1113, Argent.

SOURCE: European Journal of Biochemistry (1999), 265(1), 11-19
CODEN: EJBICAI; ISSN: 0014-2956

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Four monoclonal antibodies (mAbs) directed against the recombinant human interferon- α 2b (IFN- α 2b) were used as probes to study the interaction of the IFN mol. to its receptors. The [125I]IFN-.alpha.2b binding to immobilized mAbs was completely inhibited by IFN-.alpha.2b and IFN- α 2a but neither IFN β nor IFN γ showed any effect. Gel-filtration HPLC of the immune complexes formed by incubating [125I]IFN-.alpha.2b with paired mAbs revealed the lack of simultaneous binding of two different antibodies to the tracer, suggesting that all mAbs recognize the same IFN antigenic domain. Furthermore, the mAbs were also able to neutralize the IFN-.alpha.2b anti-viral and anti-proliferative activities as well as [125I]IFN-.alpha.2b binding to WISH cell-membranes. As [125I]mAbs did not recognize IFN exposed epitopes in the IFN:receptor complexes, mAb induction of a conformational change in the IFN binding domain impairing its binding to receptors was considered unlikely. To identify the IFN region recognized by mAbs, IFN-.alpha.2b was digested with different proteolytic enzymes. Immunoreactivity of the resulting peptides was examined by Western blot and their sequences were established by Edman degradation after blotting to poly(vinylidene difluoride) membranes. Data obtained indicated that the smallest immunoreactive region recognized by mAbs consisted of residues 107-132 or 107-146. As this zone includes the sequence 123-140, which has been involved in the binding to receptors, and the authors' mAbs did not show an allosteric behavior, it is concluded that they are directed to overlapping epitopes located close to or even included in the IFN binding domain.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 1991:360709 BIOSIS

DOCUMENT NUMBER: PREV199192048934; BA92:48934

TITLE: NATURAL HUMAN INTERFERON-ALPHA-2 IS
O-GLYCOSYLATED.

AUTHOR(S): ADOLF G [Reprint author]; KALSNER I; AHORN H; MAURER-FOGY
I; CANTELL K

CORPORATE SOURCE: ERNST-BOEHRINGER-INST, ARZNEIMITTELFORSCHUNG, BENDER AND CO
BES MBH, DR BOEHRINGER-GASSE 5-11, A-1121 VIENNA, AUSTRIA

SOURCE: Biochemical Journal, (1991) Vol. 276, No. 2, pp. 511-518.
ISSN: 0264-6021.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 13 Aug 1991

Last Updated on STN: 13 Aug 1991

AB Natural human interferon α 2 (IFN- α 2) was
isolated from a preparation of partially purified human leucocyte IFN by
monoclonal-antibody immunoaffinity chromatography. The purified protein
had a specific activity of $1.5 + 108$ i.u./mg; it was estimated to
constitute 10-20% of the total antiviral activity of leucocyte IFN.
N-Terminal amino-acid-sequence analysis identified the subspecies
IFN- α .2b and/or IFN- α 2c, whereas
not detectable. The structure of natural IFN- α 2 was found to differ
from that of its recombinant (Escherichia coli-derived) equivalent.
First, reverse-phase h.p.l.c. showed that natural IFN- α 2 was
significantly more hydrophilic than expected. Secondly, the apparent
molecular mass of the natural protein determined by SDS/PAGE was higher
than that of recombinant IFN- α 2; incubation under mild alkaline
conditions known to eliminate O-linked carbohydrates resulted in a
reduction of the apparent molecular mass to that of the recombinant
protein. On sequence analysis of proteolytic peptides, Thr-106
was found to be modified. These results suggested that Thr-106 of natural
IFN- α 2 carries O-linked carbohydrates. Reverse-phase h.p.l.c. as
well as SDS/PAGE of natural IFN- α 2 showed that glycosylation is
heterogeneous. For characterization of the carbohydrate moieties, the
protein was treated with neuraminidase and/or O-glycanase and analysed by
gel electrophoresis; in addition, glycopeptides obtained by proteinase
digestion and separated by h.p.l.c. were characterized by sequence
analysis and m.s. Further information on the composition of the glycans
was obtained by monosaccharide analysis. The results indicate that
natural IFN- α 2 contains the disaccharide galactosyl-N-
acetylgalactosamine (Gal-GalNAc) linked to the Thr-106. In part of the
molecules, this core carbohydrate carries (α -)N-acetylneuraminic
acid, whereas a disaccharide, probably N-acetyl-lactosamine, is bound to
Gal-GalNAc in another proportion of the protein. Further glycosylation
isomers are present in small amounts. As IFN- α 2 is the only
IFN- α species with a threonine residue at position 106, it may
represent the only O-glycosylated human IFN- α protein.

=> D Hist

(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007

L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTIN OR VARIANT OR MUT

L2 248 S L1 AND PROTEOL?

L3 142 DUP REM L2 (106 DUPLICATES REMOVED)

L4 21 S L3 AND RESISTANCE

L5 2141 S L1 AND (IFN -ALPHA 2B)

L6 7 S L5 AND PROTEOL?
L7 3 DUP REM L6 (4 DUPLICATES REMOVED)

=> S L5 AND glycosyl?
L8 21 L5 AND GLYCOSYL?

=> Dup Rem L8
PROCESSING COMPLETED FOR L8
L9 12 DUP REM L8 (9 DUPLICATES REMOVED)

=> D Ti L9 1-12

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
TI Treatment of interferon- α for chronic hepatitis
C

L9 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
DUPLICATE 2
TI GlycoPEGylation of recombinant therapeutic proteins produced in
Escherichia coli.

L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI Study on mechanism of interferon treating pathological scars

L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI High throughput directed evolution of proteins and peptides using
two-dimensional rational mutagenesis scanning

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions relating to isoleucine boroprolin compounds

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI Providing natural allelic variants of interferon .alpha
. as therapeutic agents with high therapeutic index

L9 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI In vitro O-glycosylation of E. coli-produced therapeutic
proteins using recombinant glycosyltransferases.

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
TI Structural characterization of N-linked and O-linked oligosaccharides
derived from interferon- α 2b and
interferon- α 14c produced by Sendai-virus-induced
human peripheral blood leukocytes

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
TI Identification of nine interferon- α subtypes
produced by Sendai virus-induced human peripheral blood leukocytes

L9 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
TI Carbohydrate composition of natural source human-leukocyte derived
interferon-alphan3.

L9 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 5
TI Expression and purification of recombinant, glycosylated human
interferon alpha 2b in murine myeloma NSo cells.

L9 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 6
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-
GLYCOSYLATED.

=> D Ibib ABS L9 1-3, 5-11

L9 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2006:507346 CAPLUS
DOCUMENT NUMBER: 145:416104
TITLE: Treatment of interferon- α
for chronic hepatitis C
AUTHOR(S): Moriyama, Mitsuhiko; Arakawa, Yasuyuki
CORPORATE SOURCE: Division of Gastroenterology and Hepatology,
Department of Medicine, Nihon University School of
Medicine, Itabashi-ku, Tokyo, 173-8610, Japan
SOURCE: Expert Opinion on Pharmacotherapy (2006), 7(9),
1163-1179
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Informa Healthcare
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Combination therapy with polyethylene glycosylated IFN- α 2a or IFN- α 2b and ribavirin is currently the standard therapy for chronic hepatitis C. However, even with this therapy, hepatitis C virus cannot be eradicated in 50% of patients with refractory chronic hepatitis C. In addition, withdrawal or dose reduction occurs in approx. 40% of patients due to adverse effects. This treatment is also a contraindication in some patients, such as in patients with coexisting diseases or in elderly patients. For these patients, standard IFN- α monotherapy is even safer and more effective. In patients with chronic hepatitis C, IFN- α monotherapy results in a significant increase in the cumulative survival rate by suppressing the progression to hepatocellular carcinoma or liver failure. In addition, other efficacious therapeutic regimens have been employed, such as prolonged administration of standard IFN- α in elderly patients; prolonged low-dose continuous administration in patients with decompensated cirrhosis or hepatocellular carcinoma postoperative patients; and combination therapy with 5-fluorouracil and standard IFN- α for advanced hepatocellular carcinoma. Monotherapy with standard IFN- α should thus be recognized as one of the important therapeutic strategies for chronic hepatitis C.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2

ACCESSION NUMBER: 2006:544386 BIOSIS
DOCUMENT NUMBER: PREV200600541473
TITLE: GlycoPEGylation of recombinant therapeutic proteins
produced in Escherichia coli.
AUTHOR(S): DeFrees, Shawn; Wang, Zhi-Guang; Xing, Ruye; Scott, Arthur E.; Wang, Jin; Zopf, David [Reprint Author]; Gouty, Dominique L.; Sjoberg, Eric R.; Panneerselvam, Krishnasamy; Brinkman-Van der Linden, Els C. M.; Bayer, Robert J.; Tarp, Mads A.; Clausen, Henrik
CORPORATE SOURCE: Neose Technol Inc, 102 Witmer Rd Dr, Horsham, PA 19044 USA
dzopf@neose.com
SOURCE: Glycobiology, (SEP 2006) Vol. 16, No. 9, pp. 833-843.
ISSN: 0959-6658.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 2006
Last Updated on STN: 18 Oct 2006

AB Covalent attachment of polyethylene glycol, PEGylation, has been shown to prolong the half-life and enhance the pharmacodynamics of therapeutic proteins. Current methods for PEGylation, which rely on chemical conjugation through reactive groups on amino acids, often generate isoforms in which PEG is attached at sites that interfere with bioactivity. Here, we present a novel strategy for site-directed PEGylation using glycosyltransferases to attach PEG to

O-glycans. The process involves enzymatic GaINAc glycosylation at specific serine and threonine residues in proteins expressed without glycosylation in Escherichia coli, followed by enzymatic transfer of sialic acid conjugated with PEG to the introduced GatNAC residues. The strategy was applied to three therapeutic polypeptides, granulocyte colony stimulating factor (G-CSF), interferon-alpha2b (IFN-alpha 2b), and granulocyte/macrophage colony stimulating factor (GM-CSF), which are currently in clinical use.

L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:714620 CAPLUS
DOCUMENT NUMBER: 146:272215
TITLE: Study on mechanism of interferon treating pathological scars
AUTHOR(S): Lu, Xin-an; Xu, Ming; Shen, Guo-liang; Lin, Wei; Zhao, Xiao-yu
CORPORATE SOURCE: Dept of Burn and Plastic Surgery, The First Hospital Affiliated to Suzhou University, Jiangsu Suzhou, 215006, Peop. Rep. China
SOURCE: Suzhou Daxue Xuebao, Yixueban (2005), 25(6), 1091-1093, 1103
CODEN: SDXYC2; ISSN: 1673-0399
PUBLISHER: Suzhou Daxue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB This paper studied the effect of interferon (IFN) on transforming growth factor- β 1 (TGF- β 1), matrix metalloprotease-1 (MMP-1), platelet-derived growth factor-BB (PDGF-BB), and glycosyltransferase (ppGalNAC-T2) in fibroblasts of pathol. scars and the mechanism of interferon on pathol. scars. The fibroblasts of pathol. scars were cultured by the method of tissue culture and were randomized in 3 groups: control (0.9% sodium chloride), low concentration (100 u/mL IFN α -2b), and high concentration (10000 u/mL IFN α -2b). The expression of TGF- β 1, MMP-1, PDGF-BB, and ppGalNAC-T2 were analyzed by RT-PCR in each group. The results showed that after treating cultured fibroblasts of pathol. scars with 100 u/mL IFN α -2b and 10000 u/mL IFN α -2b, the expression of TGF- β 1, PDGF-BB, and ppGalNAC-T2 mRNA were lower than that in the control group, and the expression of MMP-1 mRNA was higher than that of control group. The result was significantly different and was related with the concentration in the IFN α -2b. In conclusion, the cause of good effect of IFN . alpha.-2b on inhibiting fibroblast of pathol. scars may relate with some kinds of cellular factors, such as TGF- β 1 and PDGF-BB.

L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:41226 CAPLUS
DOCUMENT NUMBER: 140:105321
TITLE: Methods and compositions relating to isoleucine boroproline compounds
INVENTOR(S): Adams, Sharlene; Miller, Glenn T.; Jesson, Michael I.; Jones, Barry
PATENT ASSIGNEE(S): Point Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2004004658 | A2 | 20040115 | WO 2003-US21405 | 20030709 |

WO 2004004658 A3 20050804
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
CA 2491466 A1 20040115 CA 2003-2491466 20030709
AU 2003265264 A1 20040123 AU 2003-265264 20030709
US 2004077601 A1 20040422 US 2003-616694 20030709
US 2005084490 A1 20050421 US 2003-616409 20030709
EP 1578434 A2 20050928 EP 2003-763380 20030709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006507352 T 20060302 JP 2004-562634 20030709
CN 1802090 A 20060712 CN 2003-821282 20030709
CN 1826129 A 20060830 CN 2003-821281 20030709
IN 2005KN00151 A 20050916 IN 2005-KN151 20050208
PRIORITY APPLN. INFO.: US 2002-394856P P 20020709
US 2002-414978P P 20021001
US 2003-466435P P 20030428
WO 2003-US21405 W 20030709

OTHER SOURCE(S): MARPAT 140:105321

AB A method for treating subjects with, inter alia, abnormal cell proliferation or infectious disease using agents of formula (I, AmNHCH(CH(CH3)CH2CH3)COAlR) (where Am and Al are amino acids and R = organo boronates, organo phosphonates, fluoroalkyl ketones, alphaketos, N-peptidyl-O-(acylhydroxylamines), azapeptides, azetidines, fluoroolefins dipeptide isosteres, peptidyl (α -aminoalkyl) phosphonate esters, aminoacyl pyrrolidine-2-nitriles and 4-cyanothiazolidines) is claimed. Methods for stimulating an immune response using the compds. of the invention are also claimed. Compns. containing Ile-boroPro compds. are also provided as are kits containing the compns. The invention embraces the use of these compds. alone or in combination with other therapeutic agents.

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:39591 CAPLUS

DOCUMENT NUMBER: 140:92604

TITLE: Providing natural allelic variants of interferon α as therapeutic agents with high therapeutic index

INVENTOR(S): Escary, Jean-Louis

PATENT ASSIGNEE(S): Fr.

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2004009161 | A1 | 20040115 | US 2002-315493 | 20021210 |
| EP 1418428 | A1 | 20040512 | EP 2002-292787 | 20021107 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| CA 2413981 | A1 | 20040507 | CA 2002-2413981 | 20021211 |
| CA 2504980 | A1 | 20040521 | CA 2003-2504980 | 20031106 |
| WO 2004042394 | A2 | 20040521 | WO 2003-EP13695 | 20031106 |
| WO 2004042394 | A3 | 20040715 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
 GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
 LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
 OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
 TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2003294782 A1 20040607 AU 2003-294782 20031106
 EP 1561105 A2 20050810 EP 2003-785733 20031106
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 US 2006094641 A1 20060504 US 2005-534098 20050506
 PRIORITY APPLN. INFO.: EP 2002-292787 A 20021107
 US 2002-315493 A 20021210
 WO 2003-EP13695 W 20031106

AB Disclosed are methods for identifying and providing new therapeutic agent(s) by selecting at least one polypeptide encoded by a natural allelic variant of one preselected gene having a therapeutic potential and determining the therapeutic index of the selected polypeptide(s) and retaining as therapeutic agent(s) those polypeptide(s) whose therapeutic index is higher than that of a reference agent. The invention is illustrated by tests performed on the polypeptides encoded by natural allelic variants of 3 genes belonging to the interferon α gene family and representing: C122S IFN α -5; G45R IFN α -17; and Q114H/V127D IFN α -21 and K179E IFN α -21. The polypeptides encoded by the natural allelic variants of IFN α are subjected to several activity tests to determine their therapeutic suitability and are also compared with the product on the market, IFN α -2b (Intron A). The antiproliferative activities of the above variants were performed in tests on human lymphoblasts (Daudi cells) and their antiviral activities were evaluated in both virus-infected cell cultures (human WISH cells infection with vascular stomatitis virus) and mouse models (encephalomyocarditis virus and Friend erythroleukemia virus) of viral infection. The immunomodulatory activities of the above variants were tested on human dendritic cell maturation and a safety pharmacol. study was performed in conscious Rhesus monkeys.

L9 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 ACCESSION NUMBER: 2005:321840 BIOSIS
 DOCUMENT NUMBER: PREV200510111622
 TITLE: In vitro O-glycosylation of E. coli-produced
 therapeutic proteins using recombinant
 glycosyltransferases.
 AUTHOR(S): Defrees, Shawn [Reprint Author]; Wang, Zhi-Guang; Scott,
 Arthur E.; Wang, Jin; Xing, Ruye; Zopf, David; Gouty,
 Dominique L.; Sjoberg, Eric R.; Panneerselvam, Krishnasamy;
 Brinkman-Van der Linden, Els C. M.; Bayer, Robert J.; Tarp,
 Mads A.; Clausen, Henrik
 CORPORATE SOURCE: Neose Technol Inc, Horsham, PA USA
 SOURCE: Glycobiology, (NOV 2004) Vol. 14, No. 11, pp. 1086.
 Meeting Info.: Joint Meeting of the Society-for-
 Glycobiology/Japanese-Society-for-Carbohydrate-Research.
 Honolulu, HI, USA. November 17 -20, 2004. Soc Glycobiol;
 Japanese Soc Carbohydrate Res.
 ISSN: 0959-6658.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 25 Aug 2005
 Last Updated on STN: 25 Aug 2005

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
 ACCESSION NUMBER: 1998:266317 CAPLUS

DOCUMENT NUMBER: 129:39864
 TITLE: Structural characterization of N-linked and O-linked oligosaccharides derived from interferon-.alpha.2b and interferon-.alpha.14c produced by Sendai-virus-induced human peripheral blood leukocytes
 AUTHOR(S): Nyman, Tuula A.; Kalkkinen, Nisse; Tolo, Hannele; Helin, Jari
 CORPORATE SOURCE: Institute of Biotechnology, Protein Chemistry Lab., University of Helsinki, Finland
 SOURCE: European Journal of Biochemistry (1998), 253(2), 485-493
 CODEN: EJBCAI; ISSN: 0014-2956
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The authors have previously isolated and partially characterized the components of a highly purified interferon- α (IFN- α) preparation produced by Sendai-virus-induced human peripheral blood leukocytes. Nine IFN- α species were identified, and two of these were glycosylated. Here, the authors isolated the N-linked oligosaccharides of IFN- α 14c and the O-linked chains of IFN-.alpha.2b, and the glycans were characterized by electrospray tandem mass spectrometry and by specific glycosidase digestions monitored by matrix-assisted laser desorption ionization time of flight mass spectrometry. The IFN- α 14c N-glycans were shown to exhibit core-fucosylated biantennary glycans, with about 10% carrying an addnl. α 1,3-linked fucose unit at the antennae. The IFN-.alpha.2b was shown to carry about 50% core type-1 disialyltetrasaccharides, 30% core type-1 monosialyltrisaccharides and 20% core type-2 monosialylpentasaccharides.
 REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1998:70613 CAPLUS
 DOCUMENT NUMBER: 128:179185
 TITLE: Identification of nine interferon-.alpha. subtypes produced by Sendai virus-induced human peripheral blood leukocytes
 AUTHOR(S): Nyman, Tuula A.; Tolo, Hannele; Parkkinen, Jaakko; Kalkkinen, Nisse
 CORPORATE SOURCE: Institute of Biotechnology, Protein Chemistry Laboratory, University of Helsinki, FIN-00014, Finland
 SOURCE: Biochemical Journal (1998), 329(2), 295-302
 CODEN: BIJOAK; ISSN: 0264-6021
 PUBLISHER: Portland Press Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The human interferon- α (IFN-.alpha.) family is encoded by 13 different functional genes, and including all cloned sequence variants there are 28 potential IFN- α proteins. To find out which of the described sequences are expressed in normal human leukocytes, we have isolated and partly characterized the components of a highly purified IFN- α preparation produced by Sendai virus-induced human peripheral blood leukocytes. The identification protocol consisted of N-terminal sequencing and mass mapping of the proteins separated by reverse-phase HPLC and/or SDS/-PAGE. The highly purified leukocyte IFN- α preparation was found to contain at least nine different IFN- α species: IFN-.alpha.1a, IFN-.alpha.2b, IFN-.alpha.4b, IFN- α 7a, IFN-.alpha.8b, IFN- α 10a, IFN-.alpha.14c, IFN- α 17b, and IFN-.alpha.18b.

alpha.21b. IFN- α 1a was the major subtype, comprising approx. 30% of total leukocyte IFN- α . IFN- α 14c, the only subtype containing potential N-glycosylation sites, was shown to be glycosylated at Asn-72. Mol. mass determination of the intact proteins by electrospray ionization MS showed that there are no other post-translational modifications in the IFN- α subtypes than the glycosylation of IFN- α .2b and IFN- α 14c. Only one sequence variant was found for each subtype, suggesting that the other described gene sequences represent allelic variants or mutations that are more rarely found in the general population.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1998:58374 BIOSIS
DOCUMENT NUMBER: PREV199800058374
TITLE: Carbohydrate composition of natural source human-leukocyte derived interferon-alphan3.
AUTHOR(S): Lawrynnowicz, Witold J.; Lin, Xi; Lee, Shu-Ying; Ferencz-Biro, Katalin; Liao, Mei-June
CORPORATE SOURCE: Interferon Sci. Inc., New Brunswick, NJ 08901, USA
SOURCE: Journal of Interferon and Cytokine Research, (Oct., 1997) Vol. 17, No. SUPPL. 2, pp. S106. print.
Meeting Info.: Annual Meeting of the International Society for Interferon and Cytokine Research. San Diego, California, USA. October 19-24, 1997. International Society for Interferon and Cytokine Research.
ISSN: 1079-9907.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998

L9 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 5

ACCESSION NUMBER: 1996:331039 BIOSIS
DOCUMENT NUMBER: PREV199699053395
TITLE: Expression and purification of recombinant, glycosylated human interferon alpha 2b in murine myeloma NSo cells.
AUTHOR(S): Rossmann, Cornelia; Sharp, Nigel; Allen, Geoffrey; Gewert, Dirk [Reprint author]
CORPORATE SOURCE: Cell Mol. Biol., Astra Draco AB, P.O. Box 34, S221 00 Lund, Sweden
SOURCE: Protein Expression and Purification, (1996) Vol. 7, No. 4, pp. 335-342.
CODEN: PEXPEJ. ISSN: 1046-5928.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1996
Last Updated on STN: 27 Jul 1996

AB We have expressed recombinant human interferon-alpha -2b in mammalian cells and isolated cell lines constitutively secreting very high levels of biologically active protein. The expression system takes advantage of the strong human cytomegalovirus immediate early promoter in mouse myeloma NSo cells and glutamine synthetase as a selectable marker; spontaneous mutants with amplified gene copy numbers were selected by growth of primary transfectants in the presence of methionine sulfoximine. Using this procedure, we have isolated a recombinant NSo cell line which secretes human interferon at the rate of

20 µg/10⁶ cells/24 h and accumulates up to 120 µg/ml (approx 2.4 times 10⁻⁷ U/ml) following prolonged undiluted culture. The interferon (IFN) could be efficiently purified on a polyclonal bovine anti-human IFN-alpha specific antibody column and the glycosylation pattern was found to be similar to that of nonrecombinant IFN-alpha-2b purified from virus-induced human Namalwa cells. The biological activity of the recombinant material was indistinguishable from that of natural IFN from Namalwa cells, and the specific antiviral activity, as assayed on human HeLa cells challenged with encephalomyocarditis virus, was 2 times 10⁻⁸ IU/mg, similar to that of nonrecombinant IFN preparations. This represents the highest reported level of glycosylated, recombinant IFN expression in a stable mammalian system and is a significant advance in the large-scale production of these clinically important cytokines.

=> Log Off H

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:29:15 ON 25 MAR 2007

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAEGS1646

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *

SESSION RESUMED IN FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE'

AT 14:41:14 ON 25 MAR 2007

FILE 'BIOSIS' ENTERED AT 14:41:14 ON 25 MAR 2007

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FILE 'CAPLUS' ENTERED AT 14:41:14 ON 25 MAR 2007

COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 14:41:14 ON 25 MAR 2007

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FILE 'MEDLINE' ENTERED AT 14:41:14 ON 25 MAR 2007

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 178.38 | 178.59 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -20.28 | -20.28 |

=> D Hist

(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007

| | |
|----|---|
| L1 | 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT |
| L2 | 248 S L1 AND PROTEOL? |
| L3 | 142 DUP REM L2 (106 DUPLICATES REMOVED) |
| L4 | 21 S L3 AND RESISTANCE |
| L5 | 2141 S L1 AND (IFN -ALPHA 2B) |
| L6 | 7 S L5 AND PROTEOL? |
| L7 | 3 DUP REM L6 (4 DUPLICATES REMOVED) |
| L8 | 21 S L5 AND GLYCOSYL? |
| L9 | 12 DUP REM L8 (9 DUPLICATES REMOVED) |

=> S L1 AND ((Increased Activity)(S)antiviral)
L10 0 L1 AND ((INCREASED ACTIVITY)(S) ANTIVIRAL)

=> S L1 AND ((Increased Activity)(S)anti-proliferative)
L11 0 L1 AND ((INCREASED ACTIVITY)(S) ANTI-PROLIFERATIVE)

=> S L1 AND (Activity)(S)antiviral)
UNMATCHED RIGHT PARENTHESIS 'ANTIVIRAL)'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> S L1 AND (Activity(S)antiviral)
L12 3560 L1 AND (ACTIVITY(S) ANTIVIRAL)

=> S L1 AND (Activity(S)anti-proliferative)
L13 93 L1 AND (ACTIVITY(S) ANTI-PROLIFERATIVE)

=> Dup Rem L12
PROCESSING IS APPROXIMATELY 56% COMPLETE FOR L12
PROCESSING COMPLETED FOR L12
L14 2040 DUP REM L12 (1520 DUPLICATES REMOVED)

=> S L14 AND ((IFN-alpha 2b) OR IFNalpha-2b)
L15 71 L14 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)

=> S L13 AND ((IFN-alpha 2b) OR IFNalpha-2b)
L16 3 L13 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)

=> Dup Rem L16
PROCESSING COMPLETED FOR L16
L17 2 DUP REM L16 (1 DUPLICATE REMOVED)

=> D Ti L17 1-2

L17 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
TI Identification of a linear epitope of interferon-.alpha
.2b recognized by neutralizing monoclonal antibodies

L17 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Natural killer cell activity against cultured melanoma cells: A
dye-reduction technique with studies on augmented activity by interferon
subtypes.

=> D Ibib L17 2

L17 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:30348 BIOSIS
DOCUMENT NUMBER: PREV199395018548
TITLE: Natural killer cell activity against cultured melanoma
cells: A dye-reduction technique with studies on augmented
activity by interferon subtypes.
AUTHOR(S): Losinno, Carmela; Wines, Bruce D.; Mackay, Terrance G.
Johns And Ian R. [Reprint author]
CORPORATE SOURCE: Cent. Mol. Biol. Med., Monash Univ., Clayton, Victoria
3168, Australia
SOURCE: Natural Immunity, (1992) Vol. 11, No. 4, pp. 215-224.
ISSN: 1018-8916.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Dec 1992
Last Updated on STN: 24 Dec 1992

=> S L14 AND Proteol?

L18 15 L14 AND PROTEOL?

=> D Ti L18 1-15

L18 ANSWER 1 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Induction of APOBEC3' family proteins, a defensive maneuver underlying
interferon-induced anti-HIV-1 activity.

L18 ANSWER 2 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI TGF-beta 1 mRNA expression in liver biopsy specimens and TGF-beta 1 serum
levels in patients with chronic hepatitis C before and after antiviral
therapy.

L18 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Prolonging the half-life of human interferon-alpha2 in circulation:
Design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-
interferon-alpha2.

L18 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Hybrid (BDBB) interferon-alpha: Preformulation
studies.

L18 ANSWER 5 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI NATURAL HUMAN INTERFERON-ALPHA-2 IS O-GLYCOSYLATED.

L18 ANSWER 6 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI BIOLOGIC ACTIVITY IN A FRAGMENT OF RECOMBINANT HUMAN INTERFERON
ALPHA.

L18 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI High throughput directed evolution of proteins and peptides using
two-dimensional rational mutagenesis scanning

L18 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Proteolytic degradation of the recombinant target protein,
interferon- τ during its fermentative production in the methylotrophic
yeast, *Pichia pastoris*

L18 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI The Nonstructural NS5A Protein of Hepatitis C Virus: An Expanding,
Multifunctional Role in Enhancing Hepatitis C Virus Pathogenesis

L18 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Long-acting cytokine derivatives and their pharmaceutical compositions

L18 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification of a linear epitope of interferon-.alpha
.2b recognized by neutralizing monoclonal antibodies

L18 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Structural organization of the interferon molecules as precursors of
immuno- and neuroactive oligopeptides

L18 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Modified (1-28) beta interferons

L18 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI A new mass-spectrometric C-terminal sequencing technique finds a
similarity between γ -interferon and $\alpha 2$ -interferon and
identifies a proteolytically clipped γ -interferon that
retains full antiviral activity

L18 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon-mediated inhibition of production of Gazdar murine sarcoma
virus, a retrovirus lacking env proteins and containing an uncleaved gag

precursor

=> D Ibib Abs L18 3, 4, 13, 14

L18 ANSWER 3 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:147461 BIOSIS
DOCUMENT NUMBER: PREV200100147461
TITLE: Prolonging the half-life of human interferon-alpha2 in
circulation: Design, preparation, and analysis of
(2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon-alpha2.
AUTHOR(S): Shechter, Yoram [Reprint author]; Preciado-Patt, Liana;
Schreiber, Gideon; Fridkin, Mati
CORPORATE SOURCE: Department of Biological Chemistry, Weizmann Institute of
Science, Rehovot, 76100, Israel
yoram.shechter@weizmann.ac.il; mati.fridkin@weizmann.ac.il
SOURCE: Proceedings of the National Academy of Sciences of the
United States of America, (January 30, 2001) Vol. 98, No.
3, pp. 1212-1217. print.
CODEN: PNASA6. ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Mar 2001
Last Updated on STN: 15 Feb 2002

AB Polypeptide drugs are generally short-lived species in circulation. In
this study, we have covalently linked seven moieties of
2-sulfo-9-fluorenylmethoxycarbonyl (FMS) to the amino groups of human
interferon-alpha2. The derivative thus obtained (FMS7-IFN-alpha2) has
approx 4% the biological potency and 33 +/- 4% the receptor binding
capacity of the native cytokine. Upon incubation, FMS7-IFN-alpha2
undergoes time-dependent spontaneous hydrolysis, generating active
interferon with t1/2 values of 24 +/- 2 h at pH 8.5 and 98 +/- 10 h at pH
7.4. When native IFN- alpha2 is intravenously administered to mice,
circulating antiviral activity is maintained for a
short duration and then declines with t1/2 = 4 +/- 0.5 h, reaching
undetectable values at approx 18 h after administration. With
intravenously administered FMS7-IFN-alpha2, there is a lag period of 2 h,
followed by a progressive elevation in circulating antiviral-active
protein, which peaked at 20 h and declined with t1/2 = 35 +/- 4 h.
FMS7-IFN-alpha2 is resistant to alpha-chymotrypsin digest and to
proteolytic inactivation by human serum proteases in vitro. We
have thus introduced here an inactive IFN-alpha2 derivative, which is
resistant to in situ inactivation and has the capability of slowly
reverting to the native active protein at physiological conditions in vivo
and in vitro. Having these attributes, FMS7-IFN-alpha2 maintains
prolonged circulating antiviral activity in mice,
exceeding 7-8 times the activity of intravenously administered
native cytokine.

L18 ANSWER 4 OF 15 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:521402 BIOSIS
DOCUMENT NUMBER: PREV199900521402
TITLE: Hybrid (BDBB) interferon-alpha:
Preformulation studies.
AUTHOR(S): Allen, John D.; Bentley, David; Stringer, Rowan A.;
Lowther, Nicholas [Reprint author]
CORPORATE SOURCE: Drug Preformulation and Delivery Department, Ciba
Pharmaceuticals (now Novartis Horsham Research Centre),
Wimblehurst Road, Horsham, West Sussex, RH12 5AB, UK
SOURCE: International Journal of Pharmaceutics (Amsterdam), (Oct.
5, 1999) Vol. 187, No. 2, pp. 259-272. print.
CODEN: IJPHDE. ISSN: 0378-5173.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1999

Last Updated on STN: 3 Dec 1999

AB A number of techniques, including RP-HPLC, HP-SEC and SDS-PAGE have been used in the delineation of degradative mechanisms of recombinant hybrid (BDBB) interferon-alpha (IFN-alpha) in the solution phase. Different degradation profiles are found according to medium pH. At pH 4.0 the major routes of degradation are via chemical transformation of the monomeric protein to a species which retains antiviral activity, and by self-proteolytic hydrolysis. At pH 7.6, methionine-oxidation is the major chemical degradative process. Protein aggregation is also a significant route of degradation at the higher pH. The results have assisted in a targeted preformulation screen of potentially stabilising excipients and possible parenteral solution dosage forms have been identified. Preliminary 'real-time' storage data confirm excellent chemical and physical stability of IFN-alpha in vehicles formulated at pH 7.6 or, especially, pH 4.0 under the proposed shelf conditions.

L18: ANSWER 13 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:417791 CAPLUS

DOCUMENT NUMBER: 103:17791

TITLE: Modified (1-28) beta interferons

INVENTOR(S): Bell, Leslie D.; Boseley, Paul G.; Smith, John C.; Houghton, Michael

PATENT ASSIGNEE(S): G.D. Searle and Co., USA

SOURCE: Eur. Pat. Appl., 64 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------------------------|------|----------|-----------------|------------|
| EP 130566 | A1 | 19850109 | EP 1984-107458 | 19840628 |
| EP 130566 | B1 | 19871028 | | |
| R: BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| US 4738844 | A | 19880419 | US 1984-623814 | 19840622 |
| US 4753795 | A | 19880628 | US 1984-623601 | 19840622 |
| US 4793995 | A | 19881227 | US 1984-623815 | 19840622 |
| US 4738845 | A | 19880419 | US 1984-623894 | 19840625 |
| AU 8429981 | A | 19850103 | AU 1984-29981 | 19840628 |
| AU 577789 | B2 | 19881006 | | |
| AU 8429982 | A | 19850103 | AU 1984-29982 | 19840628 |
| AU 577790 | B2 | 19881006 | | |
| AU 8429983 | A | 19850103 | AU 1984-29983 | 19840628 |
| AU 577791 | B2 | 19881006 | | |
| AU 8429984 | A | 19850103 | AU 1984-29984 | 19840628 |
| AU 577792 | B2 | 19881006 | | |
| JP 60100599 | A | 19850604 | JP 1984-137079 | 19840702 |
| JP 60105700 | A | 19850611 | JP 1984-137081 | 19840702 |
| JP 60143000 | A | 19850729 | JP 1984-137080 | 19840702 |
| JP 60214800 | A | 19851028 | JP 1984-137078 | 19840702 |
| PRIORITY APPLN. INFO.: | | | GB 1983-17880 | A 19830701 |

AB Recombinant DNA mols. are constructed which encode modified human β -interferon (IFN- β) mols. The modification involves replacement by 3-28 amino acids of amino acids nos. 1-28, in some cases by amino acids 2-28 from α -interferon. Plasmid vectors for these modified IFN mols. are also prepared. One modified IFN- β contains serine at position 16 in place of cysteine. Other IFNs contain α -IFN sequences. These modified interferons (designated group I IFNs) display some of the following properties; greater antiproliferative or antiviral activity, modified affinity for cell surface receptors, increased therapeutic index, increased stability in proteolysis, increased solubility in vivo, and greater ease of purification or recovery from bacterial exts. Pharmaceutical compns. containing these

modified mols. are used to treat viral infections, regulate cell growth (as an antineoplastic agent), or regulate the immune system. Thus, amino acids 1-28 were replaced in groups of 3-28 amino acids by the insertion of chemical synthesized oligodeoxyribonucleotide blocks. The oligodeoxyribonucleotides were prepared by the phosphoramidate method. Blocks (30-50 bases) were assembled by combining each phosphorylated component with equimolar amts. of the unphosphorylated oligomers from the complementary strand. Plasmid vectors were then used to clone the synthetic DNA fragments into the IFN- β -coding region. The vectors also contained the Escherichia coli trp promoter. The IFN- β formed by E. coli (IFNX414) had in vitro antiviral and antiproliferative activities .apprx.5-fold higher than those of IFN- β . Another recombinant IFN- β , IFNX401 had identical antiviral and immunostimulating activity to IFN- β but is 3 times more potent in its antiproliferative activity. Other group I IFNs prepared and characterized were IFNX412, 413, 421, and modified β -.

L18 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:4461 CAPLUS

DOCUMENT NUMBER: 100:4461

TITLE: A new mass-spectrometric C-terminal sequencing technique finds a similarity between γ -interferon and $\alpha 2$ -interferon and identifies a proteolytically clipped γ -interferon that retains full antiviral activity

AUTHOR(S): Rose, Keith; Simona, Marco G.; Offord, Robin E.; Prior, Christopher P.; Otto, Berndt; Thatcher, David R.

CORPORATE SOURCE: Dep. Biochim., Cent. Med. Univ., Geneva, 1211/4, Switz.

SOURCE: Biochemical Journal (1983), 215(2), 273-7
CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB During peptide sequence mapping, it is difficult to obtain sequence information from the C-terminus ; it is much easier to obtain sequence information from the N-terminus of a protein (Rose, K., et al, 1983). A novel mass-spectrometric technique is described here which permits identification of the C-terminal peptide of a protein. This technique involves the incorporation of 180 into all α -carboxy groups liberated during enzyme-catalyzed partial hydrolysis of the protein, followed by mass spectrometry to identify as the C-terminal peptide the only peptide that did not incorporate any 180. This technique was used to identify the true C-terminal tryptic peptide of a bacterially-produced (recombinant technol.) γ -interferon (human) and to distinguish it from a peptide produced by an anomalous tryptic cleavage. A closely similar sequence segment of bacterially produced $\alpha 2$ -interferon undergoes an analogous cleavage. The C-terminus of a clipped γ -interferon that retains full antiviral activity also was identified by using the technique.

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| | |
|-----|---|
| L1 | 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTEIN OR VARIANT OR MUT |
| L2 | 248 S L1 AND PROTEOL? |
| L3 | 142 DUP REM L2 (106 DUPLICATES REMOVED) |
| L4 | 21 S L3 AND RESISTANCE |
| L5 | 2141 S L1 AND (IFN -ALPHA 2B) |
| L6 | 7 S L5 AND PROTEOL? |
| L7 | 3 DUP REM L6 (4 DUPLICATES REMOVED) |
| L8 | 21 S L5 AND GLYCOSYL? |
| L9 | 12 DUP REM L8 (9 DUPLICATES REMOVED) |
| L10 | 0 S L1 AND ((INCREASED ACTIVITY) (S) ANTIVIRAL) |
| L11 | 0 S L1 AND ((INCREASED ACTIVITY) (S) ANTI-PROLIFERATIVE) |
| L12 | 3560 S L1 AND (ACTIVITY(S) ANTIVIRAL) |
| L13 | 93 S L1 AND (ACTIVITY(S) ANTI-PROLIFERATIVE) |
| L14 | 2040 DUP REM L12 (1520 DUPLICATES REMOVED) |
| L15 | 71 S L14 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B) |
| L16 | 3 S L13 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B) |
| L17 | 2 DUP REM L16 (1 DUPLICATE REMOVED) |
| L18 | 15 S L14 AND PROTEOL? |

=> S L1(P) Protease

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L1(P) PROTEASE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L2(P) PROTEASE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L3(P) PROTEASE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L4(P) PROTEASE'
L19 837 L1(P) PROTEASE

=> Dup Rem L19

PROCESSING COMPLETED FOR L19

L20 588 DUP REM L19 (249 DUPLICATES REMOVED)

=> D Ti

L20 ANSWER 1 OF 588 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of spiroisoxazoline-based peptidomimetics as inhibitors of

serine proteases, particularly HCV NS3-NS4A protease

=> S ((INTERFERON ALPHA) OR IFN-ALPHA) (P) protease
L21 547 ((INTERFERON ALPHA) OR IFN-ALPHA) (P) PROTEASE

=> S L21 AND pd<=20020909
L22 290 L21 AND PD<=20020909

=> Dup Rem L22
PROCESSING COMPLETED FOR L22
L23 136 DUP REM L22 (154 DUPLICATES REMOVED)

=> D Ti 1-5

L23 ANSWER 1 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
TI AIDS-related Kaposi's sarcoma with chylothorax and pericardial involvement
satisfactorily treated with liposomal doxorubicin.

L23 ANSWER 2 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of recombinant protein as chaperon fusion protein

L23 ANSWER 3 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Adhesion protein, protease, and protease inhibitor mutations and methods
for diagnosis and treatment of epithelial cell adhesion-associated
diseases

L23 ANSWER 4 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of peptidomimetic protease inhibitors

L23 ANSWER 5 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of novel peptides as NS3-serine protease inhibitors of
hepatitis C virus

=> D Ti 1-136

L23 ANSWER 1 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN
TI AIDS-related Kaposi's sarcoma with chylothorax and pericardial involvement
satisfactorily treated with liposomal doxorubicin.

L23 ANSWER 2 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of recombinant protein as chaperon fusion protein

L23 ANSWER 3 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Adhesion protein, protease, and protease inhibitor mutations and methods
for diagnosis and treatment of epithelial cell adhesion-associated
diseases

L23 ANSWER 4 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of peptidomimetic protease inhibitors

L23 ANSWER 5 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of novel peptides as NS3-serine protease inhibitors of
hepatitis C virus

L23 ANSWER 6 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Novel peptides as ns3-serine protease inhibitors of hepatitis C virus

L23 ANSWER 7 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of novel imidazolidinones as NS3-serine protease inhibitors of
hepatitis C virus

L23 ANSWER 8 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Preparation of novel peptides as NS3-serine protease inhibitors of hepatitis C virus

L23 ANSWER 9 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI HIV/HCV co-infection: Clinical and therapeutic challenges.

L23 ANSWER 10 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Azapeptides as inhibitors of the Hepatitis C virus NS3 serine protease.

L23 ANSWER 11 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
 TI New therapies for the treatment of chronic hepatitis C

L23 ANSWER 12 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Ambroxol suppresses influenza-virus proliferation in the mouse airway by increasing antiviral factor levels.

L23 ANSWER 13 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2
 TI Treatment of hepatitis C.
 Original Title: Traitement de l'hepatite C.

L23 ANSWER 14 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Adverse drug reaction update.

L23 ANSWER 15 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Proteolytic degradation of the recombinant target protein, interferon- τ during its fermentative production in the methylotrophic yeast, *Pichia pastoris*

L23 ANSWER 16 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
 TI Management of protease inhibitor-associated hyperlipidemia

L23 ANSWER 17 OF 136 MEDLINE on STN
 TI Monitoring of endogenous interferon-alpha and human herpesvirus 8 in HIV-infected patients with Kaposi's sarcoma.

L23 ANSWER 18 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Preparation of macrocyclic NS3-serine protease inhibitors of hepatitis C virus comprising n-cyclic p2 moieties

L23 ANSWER 19 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Preparation of peptides as inhibitors of serine proteases, particularly hepatitis C virus NS3 protease

L23 ANSWER 20 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Efficacy of cidofovir on human herpesvirus 8 viraemia and Kaposi's sarcoma progression in two patients with AIDS.

L23 ANSWER 21 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
 TI Experimental and emerging therapies for chronic hepatitis C virus infection

L23 ANSWER 22 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
 TI Prolonging the half-life of human interferon- $\alpha 2$ in circulation: design, preparation, and analysis of (2-sulfo-9-fluorenylmethoxycarbonyl)7-interferon- $\alpha 2$

L23 ANSWER 23 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

TI Analysis of cytokine and chemokine related gene expression in peripheral blood mononuclear cells from lupus patients by DNA microarrays.

L23 ANSWER 24 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Treatment of hepatitis.

L23 ANSWER 25 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 DUPLICATE 6
 TI Treatment with interferon-alpha (IFNalpha) of hepatitis C patients induces lower serum dipeptidyl peptidase IV activity, which is related to IFNalpha-induced depressive and anxiety symptoms and immune activation.

L23 ANSWER 26 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Constraints on hepatitis C virus (HCV) NS3 serine protease genetic heterogeneity and evolution.

L23 ANSWER 27 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Hepatitis C: An update.

L23 ANSWER 28 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
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 TI Angiogenesis: Regulators and clinical applications.

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 TI Hepatitis C: Therapeutic perspectives.

L23 ANSWER 30 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 DUPLICATE 8
 TI Lowered serum dipeptidyl peptidase IV activity is associated with depressive symptoms and cytokine production in cancer patients receiving interleukin-2-based immunotherapy.

L23 ANSWER 31 OF 136 MEDLINE on STN
 TI Current and future treatment of hepatitis C.

L23 ANSWER 32 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
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 TI Activation of caspase-3 in renal cell carcinoma cells by anthracyclines or 5-fluorouracil.

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 TI Current and future treatment of hepatitis C.

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 TI Aggressive daily interferon therapy in HIV-HCV coinfecting patients.

L23 ANSWER 35 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Therapeutic uses of protease inhibitors to modulate cellular pathways and immunity

L23 ANSWER 36 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI RNase-L-dependent destabilization of interferon-induced mRNAs. A role for the 2-5A system in attenuation of the interferon response

L23 ANSWER 37 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Lack of interference between ribavirin and nucleosidic analogues in HIV/HCV co-infected individuals undergoing concomitant antiretroviral and anti-HCV combination therapy

L23 ANSWER 38 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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DUPLICATE 10
TI Localization of a receptor nonapeptide with a possible role in the binding
of the type I interferons.

L23 ANSWER 39 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 11
TI Response-adjusted α -interferon therapy for chronic hepatitis C in
HIV-infected patients

L23 ANSWER 40 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Lowered Serum Dipeptidyl Peptidase IV Activity is Associated with
Depressive Symptoms and Cytokine Production in Cancer Patients Receiving
Interleukin-2-Based Immunotherapy

L23 ANSWER 41 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Discoveries of novel biological means of controlling HIV and HIV disease

L23 ANSWER 42 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 12
TI NS3•4A protease as a target for interfering with hepatitis C virus
replication

L23 ANSWER 43 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
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TI [Coinfection with the hepatitis C virus and HIV: Current aspects].
CO-INFECTION PAR LE VIRUS DE L'HEPATITE C ET LE VIRUS DE
L'IMMUNODEFICIENCE HUMAINE: ASPECTS ACTUELS.

L23 ANSWER 44 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 13
TI Recent advances in the knowledge of biology and treatment of mastocytosis

L23 ANSWER 45 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Suppression of hepatitis C virus in human immunodeficiency virus
iron-loading anemia (HCV-HIV-ILA) patients with HAART and recombinant
human erythropoietin (r-HuEPO).

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TI STAT1 plays a protective role against the neurotoxic actions of chronic
IFN- α production in the CNS.

L23 ANSWER 47 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Plasma platelet-activating factor acetylhydrolase activity in human
immunodeficiency virus infection and the acquired immunodeficiency
syndrome

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DUPLICATE 14
TI Current and evolving therapies for hepatitis C.

L23 ANSWER 49 OF 136 MEDLINE on STN
TI Overview of interferon therapy for chronic hepatitis C.

L23 ANSWER 50 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 15
TI Hepatitis C virus: current understanding and prospects for future
therapies

L23 ANSWER 51 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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DUPLICATE 16
TI Active anti-interferon- α immunization: A European-Israeli, randomized,
double-blind, placebo-controlled clinical trial in 242 HIV-1-infected
patients (the EURIS study).

L23 ANSWER 52 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Inflammatory mediators regulate cathepsin S in macrophages and microglia:
A role in attenuating heparan sulfate interactions.

L23 ANSWER 53 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI A new contained human immunodeficiency virus type 1 host cell system for
evaluation of antiviral activities of interferons and other agents in
vitro.

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TI Systemic mastocytosis. Recent advances in diagnosis and treatment.

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TI Hepatitis c virus and human immunodeficiency virus: Clinical issues in
coinfection.

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TI Production of cytokines and metalloproteinases in rheumatoid synovitis is
T cell dependent.

L23 ANSWER 57 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Decrease of enhanced interferon alpha levels in sera of HIV-infected and
AIDS patients receiving combined antiretroviral therapy.

L23 ANSWER 58 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 21

TI Treatment strategies for chronic hepatitis C: Update since the 1997
National Institutes of Health Consensus Development Conference.

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TI Antivirals for hepatitis C virus: Challenges and prospects.

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TI Treatment strategies for chronic hepatitis C: Update since the 1997
national institutes of health consensus development Conference.

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TI Protease inhibitor and triple-drug therapy: cellular immune parameters are
not restored in pediatric AIDS patients after 6 months of treatment

L23 ANSWER 62 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Highly active antiretroviral therapy significantly improves the prognosis
of patients with HIV-associated progressive multifocal
leukoencephalopathy.

L23 ANSWER 63 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 23

TI Autocrine self-elimination of cultured ovarian cancer cells by tumor
necrosis factor α (TNF- α)

L23 ANSWER 64 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Regulation of the human protein C inhibitor gene expression in HepG2
cells: Role of Sp1 and AP2.

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TI Mastocytosis.

L23 ANSWER 66 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 25
 TI Hepatitis B and C viruses: molecular identification and targeted antiviral therapies

L23 ANSWER 67 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI alphaIFN and HIV-1 protease inhibitors (PI) inhibit HIV-8 infection: Possible therapeutic approaches for Kaposi's Sarcoma (KS).

L23 ANSWER 68 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Mechanism for differential induction of apoptosis by type I interferons.

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 TI Acquired immunodeficiency syndrome-associated Kaposi's sarcoma.

L23 ANSWER 70 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 26
 TI Pharmacokinetic studies with recombinant cytokines. Scientific issues and practical considerations

L23 ANSWER 71 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 27
 TI Obstruction of HIV-1 particle release by interferon-. alpha. occurs before viral protease processing and is independent of envelope glycoprotein

L23 ANSWER 72 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Obstruction of HIV-1 particle release by interferon-alpha occurs before viral protease processing and is independent of envelope glycoprotein.

L23 ANSWER 73 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 28
 TI Inhibition of replication of HIV in primary monocyte/macrophages by different antiviral drugs and comparative efficacy in lymphocytes.

L23 ANSWER 74 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 29
 TI A new method of "in-cell reverse transcriptase-polymerase chain reaction" for the detection of BCR/ABL transcript in chronic myeloid leukemia patients.

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 TI The role of neutrophils as mediators.

L23 ANSWER 76 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 30
 TI Induction of interleukin-6 by interferon alfa and its abrogation by a serine protease inhibitor in patients with chronic hepatitis C.

L23 ANSWER 77 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 31
 TI A phase II study of interferon-alpha, interleukin-2 and 5-fluorouracil in advanced renal carcinoma: Clinical data and laboratory evidence of protease activation.

L23 ANSWER 78 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Suppression of UV- and interferon- α -refractoriness by antipain in human IFR cells established from RSa cells sensitive to both stimuli

L23 ANSWER 79 OF 136 MEDLINE on STN
 TI Five-drug or six-drug antiretroviral therapy--conversation with Steven Scheibel, M.D. Interview by John S. James.

L23 ANSWER 80 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Suppression of saccharin-induced mutagenicity by interferon- α in human RSa cells

L23 ANSWER 81 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 32
 TI Analysis of heterogeneity of gene products (interferon) expressed in yeast.

L23 ANSWER 82 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 33
 TI In vitro inhibition of human immunodeficiency virus type 1 by a combination of delavirdine (U-90152) with protease inhibitor U-75875 or interferon-alpha.

L23 ANSWER 83 OF 136 MEDLINE on STN
 TI Immune-based therapies.

L23 ANSWER 84 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 34
 TI Inhibition of human immunodeficiency virus type 1 replication in cytokine-stimulated monocytes/macrophages by combination therapy.

L23 ANSWER 85 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 35
 TI Crystal structure of the extracellular region of human tissue factor.

L23 ANSWER 86 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 36
 TI Combination therapy for infection due to human immunodeficiency virus type 1.

L23 ANSWER 87 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Combination of peptide protease inhibitor and recombinant interferon-alpha A synergistically inhibited acute and chronic HIV-1 infection in vitro.

L23 ANSWER 88 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 37
 TI In vitro activity of inhibitors of late stages of the replication of HIV in chronically infected macrophages.

L23 ANSWER 89 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 38
 TI Analysis of mast cell subpopulations (MC(T), MC(TC)) in cutaneous inflammation using novel enzyme-histochemical staining techniques.

L23 ANSWER 90 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Structure and physicochemical properties of purified human leukocyte interferon (FPI-31)

L23 ANSWER 91 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
 TI Interferon-alpha induces plasma interleukin-6 elevation in patients with chronic hepatitis C: Its abrogation by a serine protease inhibitor.

L23 ANSWER 92 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 39
 TI Involvement of antipain-sensitive protease activity in suppression of UV-mutagenicity by human interferon-alpha

L23 ANSWER 93 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 40
TI A stress-regulated protein, GRP58, a member of thioredoxin superfamily, is
a carnitine palmitoyltransferase isoenzyme.

L23 ANSWER 94 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI Inhibition of HIV-1 replication by convergent combination therapy in
monocyte/macrophages.

L23 ANSWER 95 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 41
TI Regulation of neutrophil-derived IL-8: The role of prostaglandin E-2,
dexamethasone, and IL-4.

L23 ANSWER 96 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 42
TI Inhibition of the protease of human immunodeficiency virus blocks
replication and infectivity of the virus in chronically infected
macrophages.

L23 ANSWER 97 OF 136 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
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TI New antiretroviral agents for the therapy of HIV type-1 infection.

L23 ANSWER 98 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 43
TI Damage of tracer erythropoietin results in erroneous estimation of
concentration in mouse submaxillary gland

L23 ANSWER 99 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 44
TI Duplication of secretion signal sequences is deleterious for the secretion
of human interferon $\alpha 4$ from *Saccharomyces cerevisiae* and *Bacillus*
subtilis

L23 ANSWER 100 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 45
TI Inhibition of antigen-induced secretion in the rat jejunum by interferon
 α /beta.

L23 ANSWER 101 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI In vitro processing of fusion proteins

L23 ANSWER 102 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 46
TI Human immunodeficiency virus type 1 (HIV-1) inhibitory interactions
between protease inhibitor Ro 31-8959 and zidovudine, 2'
3'-dideoxycytidine, or recombinant interferon- α A
against zidovudine-sensitive or -resistant HIV-1 in vitro.

L23 ANSWER 103 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 47
TI FAT-STORING CELLS OF THE RAT LIVER SYNTHESIZE AND SECRETE C1 ESTERASE
INHIBITOR MODULATION BY CYTOKINES.

L23 ANSWER 104 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
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TI DIFFERENTIAL INACTIVATION OF INTERFERONS BY A PROTEASE FROM HUMAN
GRANULOCYTES.

L23 ANSWER 105 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 49
TI Rapid high level production and purification of recombinant murine and
human interferons α from *Escherichia coli*.

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| | | |
|-----|--|--|
| | STN | DUPLICATE 50 |
| TI | DIFFERENTIAL MODULATION OF TWO INTERFERON-ALPHA BINDING PROTEINS ON A HUMAN LYMPHOBLASTOID CELL LINE. | |
| L23 | ANSWER 107 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 51 |
| TI | INTERFERON INHIBITOR IN THE BLOOD OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS. | |
| L23 | ANSWER 108 OF 136 CAPLUS | COPYRIGHT 2007 ACS on STN |
| TI | Glycosylated polypeptides for better thermostability and protease resistance | |
| L23 | ANSWER 109 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 52 |
| TI | STRUCTURAL DESIGN AND MOLECULAR EVOLUTION OF A CYTOKINE RECEPTOR SUPERFAMILY. | |
| L23 | ANSWER 110 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 53 |
| TI | INTERFERON GAMMA INCREASES IN-VITRO AND IN-VIVO EXPRESSION OF C1 INHIBITOR. | |
| L23 | ANSWER 111 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 54 |
| TI | A SENSITIVE TWO-SITE ENZYME IMMUNOASSAY FOR THE DETECTION OF RAT INTERFERON-GAMMA IN BIOLOGICAL FLUIDS. | |
| L23 | ANSWER 112 OF 136 EMBASE | COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 55 |
| TI | Virologic and immunologic aspects of acquired immunodeficiency syndrome. | |
| L23 | ANSWER 113 OF 136 CAPLUS | COPYRIGHT 2007 ACS on STN |
| TI | Identification of actinophage VWB promoters and their use for expression of murine interferon alpha in Streptomyces venezuelae and S. lividans | |
| L23 | ANSWER 114 OF 136 CAPLUS | COPYRIGHT 2007 ACS on STN |
| TI | Inhibition of human natural killer cell activity by Legionella pneumophila protease | |
| L23 | ANSWER 115 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 56 |
| TI | SECRETORY EXPRESSION IN ESCHERICHIA-COLI AND BACILLUS-SUBTILIS OF HUMAN INTERFERON ALPHA GENES DIRECTED BY STAPHYLOKINASE SIGNALS. | |
| L23 | ANSWER 116 OF 136 CAPLUS | COPYRIGHT 2007 ACS on STN DUPLICATE 57 |
| TI | Mass spectrometric analysis of recombinant human α -2 interferon | |
| L23 | ANSWER 117 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 58 |
| TI | LOW TEMPERATURES STABILIZE INTERFERON ALPHA-2 AGAINST PROTEOLYSIS IN METHYLOPHILUS-METHYLOTROPHUS AND ESCHERICHIA-COLI. | |
| L23 | ANSWER 118 OF 136 | MEDLINE on STN |
| TI | [Monocyte-endothelium relations]. Relations monocytes-endothelium. | |
| L23 | ANSWER 119 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 59 |
| TI | CYTOSTATIC PRODUCTS RELEASED BY ACTIVATED MACROPHAGES UNRELATED TO INTERLEUKIN 1 TUMOR NECROSIS FACTOR ALPHA AND INTERFERON-ALPHA-BETA. | |
| L23 | ANSWER 120 OF 136 BIOSIS | COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 60 |
| TI | SELECTIVE INDUCTION OF MONONUCLEAR PHAGOCYTES TO PRODUCE NEOPTERIN BY | |

INTERFERONS.

- L23 ANSWER 121 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 61
TI THE STABILITY OF NORMAL ABNORMAL AND GENETICALLY-ENGINEERED PROTEINS IN
ESCHERICHIA-COLI STRAINS DEFICIENT IN THE LON-GENE PRODUCTS INTRACELLULAR
PROTEASE LA.
- L23 ANSWER 122 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Plasmids which include promoters for bacteriocins adapted for expression
of foreign polypeptides in Escherichia coli
- L23 ANSWER 123 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Identification and partial characterization of a novel protease in
Saccharomyces cerevisiae which cleaves the peptide bond between residues
22 and 23 in α -interferon, and identification of an
 α -interferon resistant to said proteolysis
- L23 ANSWER 124 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 62
TI INTERFERON-GAMMA IS A MAJOR REGULATOR OF C1-INHIBITOR SYNTHESIS BY HUMAN
BLOOD MONOCYTES.
- L23 ANSWER 125 OF 136 MEDLINE on STN
TI Production and function of the monocyte cytotoxic factor (MCF).
- L23 ANSWER 126 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 63
TI HUMAN MONOCYTE OR RECOMBINANT INTERLEUKIN 1'S ARE SPECIFIC FOR THE
SECRETION OF A METALLOPROTEINASE FROM CHONDROCYTES.
- L23 ANSWER 127 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 64
TI INTRACELLULAR DEGRADATION OF RECOMBINANT PROTEINS IN RELATION TO THEIR
LOCATION IN ESCHERICHIA-COLI CELLS.
- L23 ANSWER 128 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 65
TI HUMAN INTERFERON GAMMA INCREASES ADHESION OF CULTURED CARCINOMA CELLS TO
THE SUBSTRATUM.
- L23 ANSWER 129 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 66
TI A LYMPHOKINE REGULATES EXPRESSION OF ALPHA-1 PROTEINASE INHIBITOR IN HUMAN
MONOCYTES AND MACROPHAGES.
- L23 ANSWER 130 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Secretion of mature IFN- α 2 and accumulation of uncleaved precursor
by Bacillus subtilis transformed with a hybrid α -amylase signal
sequence-IFN- α 2 gene
- L23 ANSWER 131 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI An interferon-like activity released by human peripheral blood mononuclear
cells treated with inhibitors of transcription: a new type of interferon?
- L23 ANSWER 132 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
TI Interferon administration vehicles
- L23 ANSWER 133 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 67
TI MONOCLONAL ANTIBODIES ELECTROPHORETICALLY TRANSFERRED FROM POLYACRYLAMIDE
GELS RETAIN THEIR ABILITY TO BIND SPECIFIC ANTIGENS.
- L23 ANSWER 134 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 68

TI ENZYME IMMUNOASSAY OF HUMAN INTERFERON-ALPHA USING MONOCLONAL ANTIBODY.

L23 ANSWER 135 OF 136 MEDLINE on STN

TI Interferon is a polypeptide hormone.

L23 ANSWER 136 OF 136 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on
STN DUPLICATE 69

TI REDUCED SYNTHESIS OF PP-60 S-R-C AND EXPRESSION OF THE TRANSFORMATION
RELATED PHENOTYPE IN INTERFERON TREATED ROUS SARCOMA VIRUS TRANSFORMED RAT
CELLS.

=> S L23 AND (Interferon-alpha 2b)

L24 5 L23 AND (INTERFERON-ALPHA 2B)

=> D Ti 1-5

L24 ANSWER 1 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

TI Treatment of hepatitis.

L24 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

TI Treatment strategies for chronic hepatitis C: Update since the 1997
National Institutes of Health Consensus Development Conference.

L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of recombinant protein as chaperon fusion protein

L24 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of peptidomimetic protease inhibitors

L24 ANSWER 5 OF 5 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights
reserved on STN

TI Mastocytosis.

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For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> log off h

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PASSWORD:

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 FILE 'MEDLINE' ENTERED AT 16:09:18 ON 25 MAR 2007

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 340.59 | 340.80 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | -26.52 | -26.52 |

=> D Hist

(FILE 'HOME' ENTERED AT 13:34:30 ON 25 MAR 2007)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE' ENTERED AT 13:34:48 ON 25 MAR 2007

L1 70256 S (INTERFERON ALPHA) OR IFN-ALPHA AND (MUTIN OR VARIANT OR MUT
 L2 248 S L1 AND PROTEOL?
 L3 142 DUP REM L2 (106 DUPLICATES REMOVED)
 L4 21 S L3 AND RESISTANCE
 L5 2141 S L1 AND (IFN -ALPHA 2B)
 L6 7 S L5 AND PROTEOL?
 L7 3 DUP REM L6 (4 DUPLICATES REMOVED)
 L8 21 S L5 AND GLYCOSYL?
 L9 12 DUP REM L8 (9 DUPLICATES REMOVED)
 L10 0 S L1 AND ((INCREASED ACTIVITY) (S) ANTIVIRAL)
 L11 0 S L1 AND ((INCREASED ACTIVITY) (S) ANTI-PROLIFERATIVE)
 L12 3560 S L1 AND (ACTIVITY(S) ANTIVIRAL)
 L13 93 S L1 AND (ACTIVITY(S) ANTI-PROLIFERATIVE)
 L14 2040 DUP REM L12 (1520 DUPLICATES REMOVED)
 L15 71 S L14 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)
 L16 3 S L13 AND ((IFN-ALPHA 2B) OR IFNALPHA-2B)
 L17 2 DUP REM L16 (1 DUPLICATE REMOVED)
 L18 15 S L14 AND PROTEOL?
 L19 837 S L1(P) PROTEASE
 L20 588 DUP REM L19 (249 DUPLICATES REMOVED)
 L21 547 S ((INTERFERON ALPHA) OR IFN-ALPHA) (P) PROTEASE
 L22 290 S L21 AND PD<=20020909
 L23 136 DUP REM L22 (154 DUPLICATES REMOVED)
 L24 5 S L23 AND (INTERFERON-ALPHA 2B)

=> D L23 Ibib Abs 108, 116, 123

L23 ANSWER 108 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1991:137408 CAPLUS
 DOCUMENT NUMBER: 114:137408
 TITLE: Glycosylated polypeptides for better thermostability
 and protease resistance
 INVENTOR(S): Sasaki, Katsutoshi; Nishi, Tatsunari; Yasumura,
 Shigeyoshi; Sato, Moriyuki; Itoh, Seiga
 PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan
 SOURCE: Eur. Pat. Appl., 130 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 370205 | A2 | 19900530 | EP 1989-117981 | 19890928 <-- |
| EP 370205 | A3 | 19900613 | | |
| EP 370205 | B1 | 19980722 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| US 5218092 | A | 19930608 | US 1989-413482 | 19890927 <-- |
| JP 02227075 | A | 19900910 | JP 1989-253097 | 19890928 <-- |
| JP 2928287 | B2 | 19990803 | | |
| AT 168699 | T | 19980815 | AT 1989-117981 | 19890928 <-- |
| ES 2121734 | T3 | 19981216 | ES 1989-117981 | 19890928 <-- |
| CA 1341385 | C | 20020820 | CA 1989-614003 | 19890928 <-- |

PRIORITY APPLN. INFO.:

JP 1988-245705 A 19880929

AB Physiol. active polypeptide-encoding gene is mutagenized such that ≥ 1 new glycosylation sites (markush structure given) are formed. The gene is introduced by transformation into, e.g. CHO cells, to produce glycosylated physiol. active polypeptides, e.g. urokinase, containing ≥ 1 new carbohydrate chains. Plasmid pAS28 encoding glycosylated human granulocyte colony stimulating factor hG-CSF[ND28] was constructed and introduced into CHO cells for production. The recombinant hG-CSF[ND28] was a mixture of singly and doubly O-glycosylated forms. The recombinant hG-CSF[ND28] mixture had a better protease-resistance than that of the wild type hG-CSF; and hG-CSF[ND28] having 2 carbohydrate chains had better protease-resistance than that having only one. Glycosylated hG-CSF, hG-CSF[ND28N6], had better thermostability at 56° than the nonglycosylated counterpart obtained by N-glycanase treatment. Glycosylated urokinase, similarly, was prepared. Like natural prourokinase, it scarcely activated the systemic fibrinolytic system; and it had less sensitivity to thrombin and a prolonged plasma elimination half-life (.apprx.2-fold).

L23 ANSWER 116 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 57

ACCESSION NUMBER: 1989:590765 CAPLUS

DOCUMENT NUMBER: 111:190765

TITLE: Mass spectrometric analysis of recombinant human α -2 interferon

AUTHOR(S): Padron, G.; Besada, V.; Agraz, A.; Quinones, Y.; Herrera, L.; Shimonishi, Y.; Takao, T.

CORPORATE SOURCE: Cent. Genet. Eng. Biotechnol., Havana, Cuba

SOURCE: Analytica Chimica Acta (1989), 223(2), 361-9

CODEN: ACACAM; ISSN: 0003-2670

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mass spectrometry (MS) was used for the characterization of recombinant human α -2 interferon (α -2 IFN) produced in *Escherichia coli*. After purification by monoclonal antibody affinity chromatog., α -2 IFN showed two major peaks in reversed-phase liquid chromatog. (RP-LC). Each component was digested with trypsin and *Staphylococcus aureus* protease V8, sep. or in tandem, and the peptide mixture was analyzed by MS without further purification. The first peak corresponded to the 165 amino acid sequence of human α -2 IFN and the main component of the second peak was the acetylated Cys1 α -2 IFN. It was also possible to verify by MS the location of the S-S bonds in α -2 IFN and the occurrence of incorrect S-S bridges in the products of some renaturation processes. The best renaturation process for obtaining a product without adducts or scrambling of disulfide bonds could be found by using RP-LC and fast-atom-bombardment MS.

L23 ANSWER 123 OF 136 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1988:144742 CAPLUS

DOCUMENT NUMBER: 108:144742

TITLE: Identification and partial characterization of a novel

protease in *Saccharomyces cerevisiae* which cleaves the peptide bond between residues 22 and 23 in α -interferon, and identification of an α -interferon resistant to said proteolysis

INVENTOR(S): O'Loughlin, John T.
 PATENT ASSIGNEE(S): Interferon Sciences, Inc., USA
 SOURCE: Eur. Pat. Appl., 20 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|--------------|
| EP 240224 | A2 | 19871007 | EP 1987-302519 | 19870324 <-- |
| EP 240224 | A3 | 19890201 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| DK 8701614 | A | 19871001 | DK 1987-1614 | 19870330 <-- |
| CN 87102497 | A | 19871111 | CN 1987-102497 | 19870330 <-- |
| JP 62296892 | A | 19871224 | JP 1987-74566 | 19870330 <-- |
| PRIORITY APPLN. INFO.: | | | US 1986-845937 | A 19860331 |

AB A novel *S. cerevisiae* protease cleaves α -interferons between basic amino acids at positions 22 and 23, but cleavage does not occur if residue 22 is serine. A recombinant interferon α with serine, threonine, asparagine, glutamine, or glycine at position 22 could be produced intact in a microorganism whose primary proteolytic activity against the natural species is at that site. The protease was partially purified from a protease-deficient PEP 3-4 *S. cerevisiae* mutant. It was membrane-bound and activated by the Triton X-100 present during cell lysis. Recombinant interferons α -1, α -2, and α -8 were all incubated with the protease. Both α -2 and α -8 were cleaved between amino acids 22 and 23 (which were Arg-Lys and Arg-Arg, resp.), but α -1 (Ser-Arg) was not.

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|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 350.02 | 350.23 |

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SINCE FILE
ENTRY
-28.86

TOTAL
SESSION
-28.86

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